

Unexpected Role of the Ru(II) Orbital and Spin Contribution on Photoinduced Ligand Exchange: New Mechanism To Access the Photodynamic Therapy Window

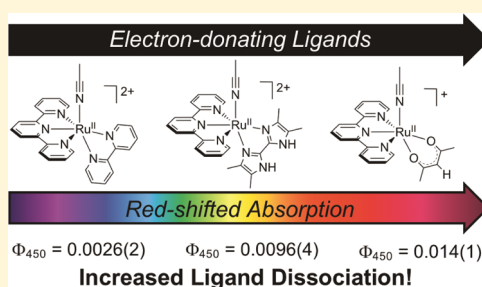
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ABSTRACT: A series of 12 Ru(II) complexes of the type [Ru(tpy)(L)]ⁿ⁺, 1–12, containing the tridentate tpy ligand (tpy = 2,2':6',2''-terpyridine) and various bidentate ancillary ligands, L, were synthesized and evaluated for their ability to photodissociate CH₃CN, a model for nitrile-containing drugs. Although the bidentate ligands chosen display a similar degree of steric bulk around the metal center in the ground state, the photosubstitution efficiencies of 1–12 vary by approximately an order of magnitude. The complexes containing the most electron-donating bidentate ligands, 8–11, exhibit the larger quantum yield values for ligand exchange in water. Complexes 8–11 also possess the smallest energy gap between the ground state and the lowest energy metal-to-ligand charge-transfer (³MLCT) excited state, and density functional theory calculations show that a large degree of the ligand character is present in their highest occupied molecular orbitals (HOMOs) and in their ³MLCT excited states. These results show that ligand mixing affects the π -back-bonding ability of the metal center in the excited state, increasing the quantum yields of nitrile ligand dissociation. Linear relationships were observed between the quantum yield of ligand dissociation and both the Mulliken spin density on the metal center in the excited state and the percent of the Ru(d) character in the ground-state HOMO. These findings, driven by the presence of π -donating ancillary ligands that enhance excited-state reactivity, can be used to design new complexes with greater quantum yields for the release of nitrile-containing drugs and biological probes without affecting their stability in the dark.



INTRODUCTION

Ruthenium polypyridyl complexes have long been of interest for use in a wide range of applications, including solar energy conversion, water oxidation catalysis, molecular switches, biological sensors, and photoredox catalysis, among others.^{1–26} The wide range of applications of these types of complexes is due to their unique and highly tunable excited-state properties, typically characterized by relatively strong absorption throughout the visible range, intense emission, and long-lived triplet metal-to-ligand charge-transfer (³MLCT) excited states. In these complexes, the properties of the ³MLCT states can be readily tuned by synthetic modification of the ligands around the metal center.^{27,28} For example, previous works on 2,2'-bipyridine (bpy) complexes of Ru(II) showed that in many cases, the emission of these complexes does not occur from a "pure" ³MLCT state. Rather, density functional theory (DFT) calculations suggest that bpy-based orbitals mix with the Ru(d π)-based singly occupied molecular orbital in the ³MLCT state, resulting in a greater degree of mixing of the $\pi\pi^*$ character into the ³MLCT excited state. Of the compounds investigated, this effect was most pronounced in [Ru(bpy)₂(CH₃CN)₂]²⁺ and [Ru([9]aneS₃)(bpy)(CN)]⁺, where

[9]aneS₃ = 1,4,7-trithiacyclononane.²⁹ Additional modeling of emission spectra of [Ru(bpy)(L)₃]ⁿ⁺ and [Ru(bpy)₂(L)₂]ⁿ⁺, where L represents a wide variety of mono- and bidentate ligands, showed that the lowest energy ³MLCT states of complexes that absorb or emit at energies that fall within or near the near-infrared (NIR) region tend to possess less charge-transfer (CT) character and more ligand-based $\pi\pi^*$ character. This mixing between Ru(d π) orbitals and bpy(π^*) orbitals leads to a lower degree of the metal character in the highest occupied molecular orbital (HOMO) of the ground state.^{30,31}

Recently, the field of photochemotherapy (PCT) has evolved as one potential application of polypyridyl Ru(II) complexes that has very different excited-state requirements than sensing and solar energy conversion. The latter requires a long-lived, emissive ³MLCT state, whereas it has long been postulated that efficient photoinduced ligand dissociation for the release of biologically active drugs or probes with

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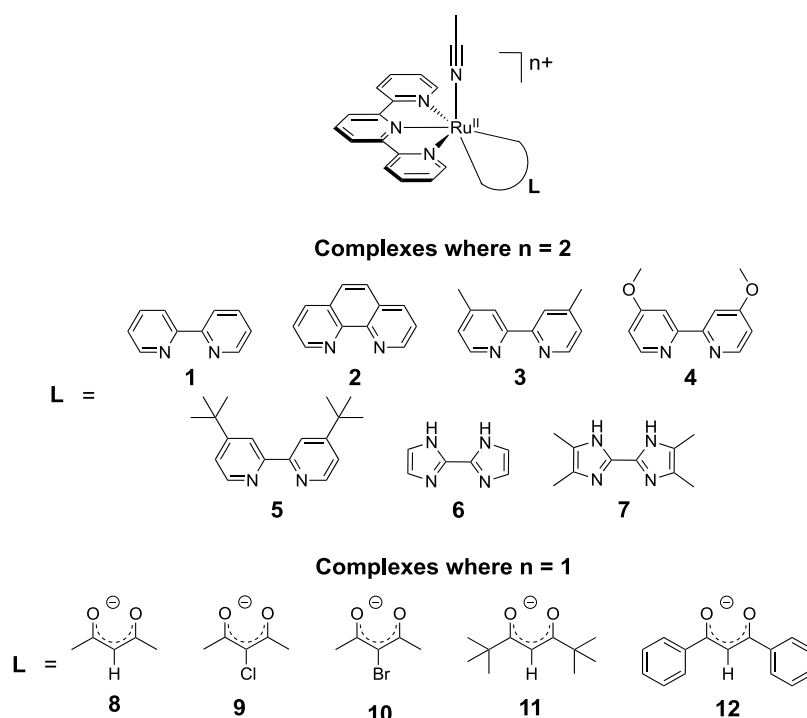


Figure 1. Schematic representation of the complex structure and the bidentate ligands, L.

68 spatiotemporal control necessitates the population of non-
 69 emissive, dissociative metal-centered ligand-field (^3LF)
 70 states.^{32–40} Presently, much of the work in the field has
 71 centered on increasing photosubstitution quantum yields by
 72 introducing steric bulk pointed toward the metal, resulting in
 73 distortions from the pseudo-octahedral geometry around the
 74 Ru(II) center in the ground-state structure that lower the
 75 energies of the ^3LF excited states.^{32,34,41–46} However, recent
 76 work by our group on a series of Ru(II) complexes containing
 77 tetradentate ligands related to tris(2-pyridylmethyl)amine
 78 revealed that of the four complexes investigated, the only
 79 one that possessed a mixed $^3\text{MLCT}/^3\pi\pi^*$ state as the lowest
 80 energy triplet state has a quantum yield of ligand dissociation
 81 that is $\sim$ five-fold greater than that of the analogous complex
 82 without a heavily mixed $^3\text{MLCT}$ state.⁴⁷

83 The surprisingly wide range of photosubstitution reactivities
 84 displayed by closely related types of complexes,^{35,45,46,48–50}
 85 coupled with the desire to synthesize compounds that absorb
 86 in the “photodynamic therapy (PDT) window” from 600 to
 87 900 nm,^{51,52} have made the rational design of Ru(II)
 88 complexes that are well suited for PCT difficult to date.
 89 Additionally, it has been generally believed that complexes with
 90 low-energy MLCT states that could absorb in this PDT
 91 window would not be able to undergo efficient ligand
 92 dissociation, as the energy gap between MLCT and
 93 dissociative LF states would be too large.^{35–39,49,53,54}

94 The present work focuses on the investigation of the
 95 photoinduced ligand exchange of a series of relatively
 96 unstrained $[\text{Ru}(\text{tpy})(\text{L})(\text{CH}_3\text{CN})]^{n+}$ complexes (Figure 1),
 97 where tpy = 2,2':6',2''-terpyridine and the neutral ligands L are
 98 2,2'-bipyridine (bpy, 1), 1,10-phenanthroline (phen, 2), 4,4'-
 99 dimethyl-2,2'-bipyridine (4,4'-Me₂bpy, 3), 4,4'-dimethoxy-
 100 2,2'-bipyridine (4,4'-(MeO)₂bpy, 4), 4,4'-di-tert-butyl-2,2'-
 101 bipyridine (4,4'-t-Bu₂bpy, 5), 1H,1'H-2,2'-biimidazole (bim,
 102 6), and 4,4',5,5'-tetramethyl-1H,1'H-2,2'-diimidazole
 103 (Me₄bim, 7), for which $n = 2$, while the anionic ligands L

utilized are acetylacetonate (acac, 8), 3-chloroacetylacetonate
 (Cl-acac, 9), 3-bromoacetylacetonate (Br-acac, 10), 2,2,6,6-
 tetramethyl-3,5-heptanedionate (thd, 11), and 1,3-diphenyl-
 1,3-propanedione (DBM, 12), for which $n = 1$. Complexes 1–
 12 exhibit a wide range of photosubstitution efficiencies,
 despite the similarity in steric bulk afforded by the ancillary
 ligands throughout the series. DFT provided information on
 the excited states and bonding of 1–12, and it was used to
 relate the calculated Mulliken spin density (MSD) on the
 ruthenium metal center in the lowest energy triplet state with
 the quantum yield of ligand exchange. In contrast to
 expectation, the complexes with the lowest metal character
 and spin density in the lowest energy triplet state are the most
 photoactive. Importantly, counter to the commonly accepted
 notion that complexes with low-energy $^3\text{MLCT}$ states do not
 possess sufficient energy to populate the dissociative ^3LF states
 and undergo ligand exchange,^{35,53} and the four most active
 complexes of the series, 8–11, exhibit the most red-shifted
 $^1\text{MLCT}$ absorption maxima.⁵⁵ These relationships can serve as
 a powerful tool to predict the photochemical activity of a
 related series of analogous complexes, and shows that efficient
 ligand photodissociation in the PDT window is attainable
 without sacrificing thermal stability or photoreactivity. The
 present work highlights the importance of metal/ligand orbital
 mixing on photophysical properties and points to the
 complexity of the excited-state reactivity of Ru(II) complexes.
 Moreover, it reveals a new strategy for the design of ruthenium
 complexes for the photoinduced release of therapeutics and
 diagnostic molecular probes.

RESULTS AND DISCUSSION

Synthesis and X-ray Crystallography. Complexes 1–12
 were synthesized from two well-known starting materials,
 either $[\text{Ru}(\text{tpy})\text{Cl}_3 \cdot 3\text{H}_2\text{O}]$ or the $[\text{Ru}(\eta^6\text{-p-cymene})(\mu\text{-Cl})\text{Cl}]_2$
 dimer to form the appropriate $[\text{Ru}(\text{p-cymene})(\text{L})\text{Cl}]$ complex
 (Supporting Information, Figures S1–S16). In both cases, the

synthetic procedures allow for the stepwise installation of the ligands in a fashion that greatly reduces the formation of by products and renders the desired product easily purified from any homoleptic complexes formed. All complexes were obtained in moderate to good yields.

The X-ray crystal structure of **4** is shown in Figure 2a and is similar to that of its parent complex **1** and related 4,4'-

of **4** (Table 1),⁵⁶ while the similar bite angle of the bidentate ligand and tilt angle of the CH₃CN ligand indicate a similar degree of steric distortion that can be found between **1** and **4** (Table 1), as expected.

The X-ray crystal structure of **7** is shown in Figure 2b. Despite the presence of the two methyl groups adjacent to the coordinated N atoms, the Ru–N bond lengths, the bite angle of the bidentate ligand, and the tilt angle of the coordinated CH₃CN ligand in **7** are very similar to those observed in **1** (Table 1),⁵⁶ suggesting a similar degree of steric hindrance present in the ground state between the two complexes. At 2.118 and 2.103 Å, the Ru–N bonds to the Me₄bim ligand in **7** are slightly elongated compared to the Ru–N bonds in the bpy-based complexes (Table 1); however, they are similar to those observed in related biimidazole-containing complexes without the methyl groups present and therefore are not indicative of steric strain in the coordination sphere (see Table S8 and references therein).

The X-ray crystal structure of **12** (Figure 2c, Table 2) is similar to that of its parent complex **8** (Tables S10–S14).⁵⁵ The addition of the phenyl rings to the bidentate ligand in **12** does not have a significant effect on its ground-state structure, as these groups are pointed away from the metal center and do not add additional steric distortion, as evidenced by the nearly identical tilt angle of the CH₃CN ligand in **12** as compared to that of **8** (Table 2). It is interesting to note, however, that the bite angle of the bidentate ligand in the acac-based complexes is closer to ideal octahedral geometry, ~90°, than in the complexes derived from bpy, ~80° (Tables 1 and 2), indicating that there should be a lesser degree of steric distortion and slightly better orbital overlap present in **8**–**12** than in **1**–**5**.

Photochemistry. The electronic absorption spectra of **1**–**5** (Figure S17) are typical of diimine Ru(II) complexes containing tpy, with a moderately intense mixed MLCT transition of both Ru(dπ) → bpy/phen(π*) and Ru(dπ) → tpy(π*) characters at ~455–458 nm and a low-energy shoulder at ~570–585 nm that is Ru(dπ) → tpy(π*) in nature (Table 3).^{57,58} In these complexes, the electron withdrawing/donating character of the substituent in the 4,4'-positions of the bipyridine ligand has only a slight influence on the energy of the most intense ¹MLCT transition. Complexes **6** and **7** exhibit similar absorption spectra (Figure S18, Table 3), with ¹MLCT transition centered at ~465 nm that is Ru(dπ) → tpy(π*) in character. However, the introduction of the biimidazole-type bidentate ligand in these complexes leads to more pronounced and red-shifted Ru(dπ) → tpy(π*) shoulders at ~550 and 600 nm (Table 3). The presence of the more electron-donating acac and electron-substituted acac bidentate ligand in **8**–**12** destabilizes the Ru(dπ) set and red-shifts the absorption into the PDT window 200

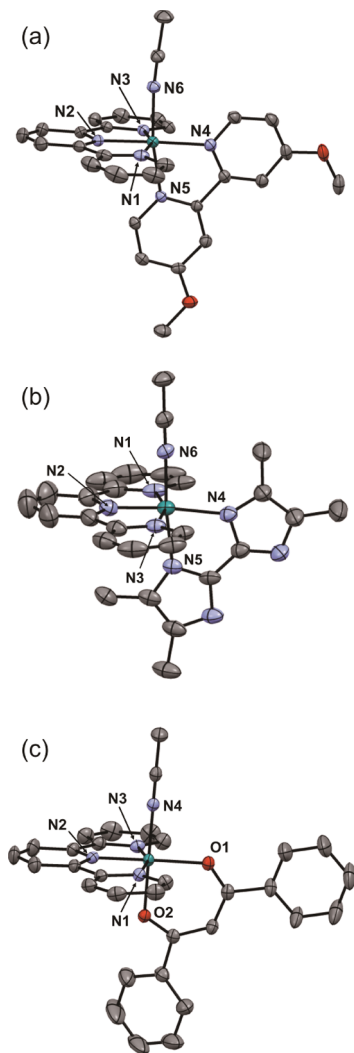


Figure 2. Oak Ridge thermal ellipsoid plots of (a) **4**, (b) **7**, and (c) **12** (ellipsoids drawn at 50% probability and hydrogen atoms have been omitted for clarity); Ru: cyan, N: light blue, C: gray, and O: red.

substituted bpy complexes (see Tables S3–S7 and references therein). The similar bond lengths between **1** and **4** indicate that the methoxy substituents in the 4,4' positions of the bpy ring have little influence on the overall ground-state structure

Table 1. Selected Bond Lengths (Å) and Angles (deg) in **1**,⁵⁶ **4**, and **7**

	Ru–N bond						bidentate bite angle	
	N1	N2	N3	N4	N5 ^a	N6 ^b	N4–Ru–N5	CH ₃ CN tilt angle ^c
1	2.063(8)	1.953(8)	2.077(8)	2.062(8)	2.038(9)	2.03(1)	79.2(3)	169.8(9)
4	2.071(2)	1.970(2)	2.080(2)	2.074(2)	2.054(2)	2.032(2)	78.28(8)	173.3(2)
7	2.067(9)	1.945(4)	2.064(3)	2.118(3)	2.103(3)	2.023(3)	78.5(1)	178.4(3)

^aAtom positioned trans to the CH₃CN ligand. ^bCH₃CN. ^cThe CH₃CN tilt angle is defined as the angle from Ru–N6–C*; C* represents the carbon atom adjacent to N6 in CH₃CN (C26 in **1**, C28 in **4**, and C26 in **7**).

Table 2. Selected Bond Lengths (Å) and Angles (deg) in **8**⁵⁵ and **12**

	Ru–N bond				Ru–O bond		bidentate bite angle	CH ₃ CN tilt angle ^c
	N1	N2	N3	N4 ^a	O1	O2 ^b	O1–Ru–O2	
8	2.069(2)	1.939(1)	2.056(2)	2.014(2)	2.080(1)	2.056(1)	91.50(6)	177.2(2)
12	2.063(3)	1.945(3)	2.070(4)	2.015(4)	2.078(2)	2.037(3)	90.8(1)	176.7(3)

^aCH₃CN. ^bAtom positioned trans to CH₃CN. ^cThe CH₃CN tilt angle is defined as the angle from Ru–N4–C*; C* represents the carbon atom adjacent to N4 in CH₃CN (C21 in **8** and C31 in **12**).

Table 3. Photochemical, Photophysical, and Electronic Structure Data for **1–12**

	$\lambda_{\text{max}}/\text{nm}$ ($\epsilon/\times 10^3 \text{ M}^{-1} \text{ cm}^{-1}$) ^a	$\lambda_{\text{em}}/\text{cm}^{-1}$ ^b	$\Phi_{450}(\text{H}_2\text{O})^c$	$\Phi_{450}(\text{Cl})^d$	¹ GS HOMO	MSD– ³ MLCT	
					% Ru d	Ru	tpy
1	455 (10.4)	16Å600	0.0026(2) ^e	0.0062(1)	76.3	0.881	0.909
2	455 (11.0)	16Å600	0.0053(1)		76.1	0.878	0.983
3	456 (9.9)	16Å100	0.0031(3)	0.0049(1)	76.1	0.882	0.989
4	458 (8.8), 530 (1.7), 585 (0.7)	15Å700	0.0048(3)		73.2	0.870	1.04
5	455 (10.4), 515 (1.8), 570 (0.6)	16Å100	0.0022(1)		75.8	0.886	1.07
6	465 (5.4), 545 (1.6), 600 (0.9)	15Å100	0.0035(2)		74.8	0.882	1.08
7	468 (5.7), 555 (1.6), 620 (0.8)	14Å600	0.0096(4)		61.2	0.813	1.06
8	530 (5.8)	13Å100	0.014(1) ^f	0.026(1)	61.3	0.804	1.05
9	519 (5.5)	13Å600	0.018(1) ^f		48.3	0.741	1.04
10	521 (5.4)	13Å700	0.016(1) ^f	0.027(1)	47.1	0.738	1.04
11	535 (5.9)	13Å000	0.015(1) ^f	0.022(1)	58.8	0.786	1.04
12	522 (7.4)	13Å300	0.0012(1)	0.021(1)	58.2	0.785	1.04

^aAcetone. ^bFrom emission in CH₃CN at 77 K; diimine complexes are weakly emissive at 298 K and acac derivatives were weakly luminescent at 77 K. ^cH₂O (<5% acetone) at 298 K. ^dCH₂Cl₂ with 10 mM Bu₄NCl at 298 K. ^eFrom ref 59. ^fFrom ref 55.

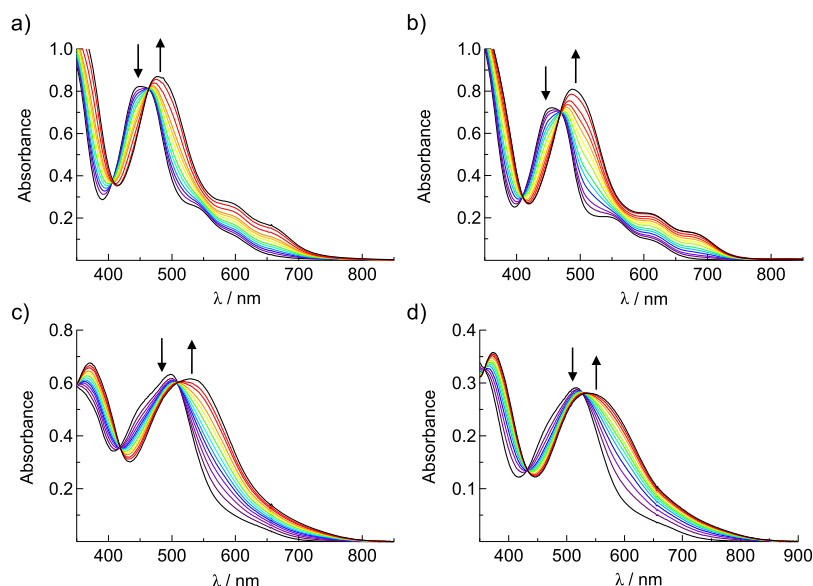


Figure 3. Changes in the electronic absorption spectra upon irradiation with 655 nm of (a) **6** from 0 to 30 min, (b) **7** from 0 to 16 min, (c) **9** from 0 to 160 s, and (d) **11** from 0 to 100 s in H₂O (<5% acetone).

(Figure S19), with ¹MLCT transitions between 519 and 535 nm and Ru(dπ) → tpy(π*) shoulders at ~700 nm (Table 3).⁵⁵

Irradiation of these complexes with $\lambda_{\text{irr}} \geq 395$ nm in water (<5% acetone) leads to the expected red shift of the MLCT absorption as the CH₃CN ligand exchanges with the weaker-field OH₂ ligand and forms the respective aqua complex (Figure S20).^{55,59} Complexes **1–12** are stable in water (<5% acetone) in the dark for at least 3 h (Figure S21). Complexes **6–11** are unique in that their red-shifted transitions place a considerable amount of absorption in the PDT window,

allowing for efficient photodissociation using 655 nm LEDs on a practical timescale (Figure 3).

Quantum yields of ligand exchange for **1–12** were measured in H₂O (<5% acetone) using $\lambda_{\text{irr}} = 450$ nm (Φ_{450}), and the resulting values span an order of magnitude. Complex **12** exhibits the lowest quantum yield, $\Phi_{450} = 0.0012(1)$, and **9** exhibits the highest, $\Phi_{450} = 0.018(1)$ (Table 3). The quantum yields for **7–11** were unexpectedly high, given their red-shifted absorption spectra, while that for **12** was lower than expected, given the structural similarities to its acac parent complex, **8**, and other acac derivatives **9–11**. This large range in

photodissociation efficiency was surprising, as crystal structures or DFT-optimized structures of 1–12 (Tables 1 and 2 and S3–S14) show no discernible differences in the amount of steric distortion around the metal center in the ground state that is well known to affect the relative energy of the ³LF states thought to be responsible for ligand photodissociation.^{41,42} This finding suggests that other electronic factors in either the ground state or excited state may play a significant role in the efficiency of photoinduced ligand exchange in this series of complexes.

Ground-State Electronic Structure Calculations. In an effort to understand the observed photochemical trends, electronic structure calculations were undertaken. Geometry optimizations for 1–12 in the singlet ground state produced structures in good agreement with crystallographic data and calculated $\nu(\text{CN})$ stretches consistent with experimental values (Tables S3–S14). The electronic structure of these complexes in the ground state can be described by the frontier molecular orbitals, which are similar across the series (Figures S22–S24). The HOMOs of 1–12 are mostly composed of Ru d character with varying degrees of ligand mixing, while the lowest unoccupied molecular orbitals (LUMOs) are nearly exclusively localized on the tpy ligand. Representative orbital contours for the HOMOs and LUMOs of complexes 2 and 8 are shown in Figure 4. It is evident from Figure 4a that the HOMO of 2 is

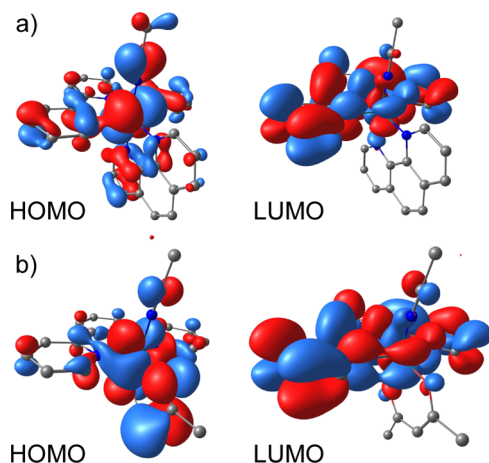


Figure 4. Molecular orbital contours of (a) 2 and (b) 8 (drawn at an isovalue of 0.02).

localized on the metal with little contribution from the ligands, whereas Figure 4b shows extensive Ru-acac mixing leading to significant localization of the HOMO of 8 on the acac ligand. The LUMOs of 2 and 8 are localized on the tpy ligand. The HOMOs and LUMOs of 1–12 are compared in Figures S22–S24, and the calculated percent contribution of the Ru d-orbital to the HOMO of each complex in the singlet ground state, ¹GS, is listed in Table 3.

It is evident from the data presented in Table 3 that, with the exception of 12, the complexes with higher quantum yields of ligand exchange in water, $\Phi_{450}(\text{H}_2\text{O})$, are calculated to possess a lower amount of Ru d character in the HOMO, % Ru(d). In fact, a plot of $\Phi_{450}(\text{H}_2\text{O})$ versus % Ru(d) results in a linear relationship (Figure 5), suggesting that ligand mixing in the HOMO is important for efficient ligand dissociation. A significant degree of the ligand character has previously been shown to have a dramatic impact on the efficiency of

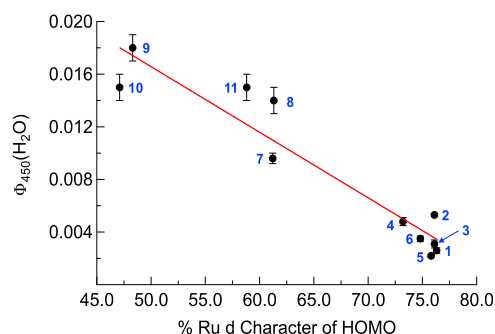


Figure 5. Plot of the measured $\Phi_{450}(\text{H}_2\text{O})$ vs the calculated percentage of Ru d character in the ground-state HOMO of 1–11; the data can be fit to a line with $R^2 = 0.90$.

photoinduced ligand dissociation of nitriles in other types of polypyridyl Ru(II) complexes.⁴⁷

MSDs in the Triplet Excited State. Geometry optimizations and vibrational frequency calculations of 1–12 were also completed in the triplet excited state (Tables S3–S14). All complexes show elongated Ru–N(CH₃CN) bonds in the triplet excited state as compared to the ground state. MSD calculations were performed to determine the spin density on the Ru(II) center and to examine the nature of the triplet excited state. For complexes with a ³MLCT state as the lowest energy triplet state, the MSD on the Ru(II) center should theoretically equal one, indicating exactly one unpaired electron on the metal. Complexes with a ³LF state as the lowest energy triplet state should have a spin density of two on the Ru center, consistent with the presence of two unpaired electrons on the metal. Any complex with a spin density on the metal that is not precisely one or two suggests some degree of metal/ligand mixing. For 1–12, the MSD on the Ru(II) center was calculated to be less than one, with some complexes exhibiting a significant amount of Ru(II) mixing with both the tpy and bidentate ligands. The calculated MSD values for 1–12 in the triplet state on Ru and on the tpy ligand are listed in Table 3, and the values indicate that the lowest energy triplet excited state is MLCT in nature with a significant amount of the ligand character. Figure 6 compares the MSD values on the metal and the ligands of the ³MLCT state of 1, 6, and 8.

A linear relationship was also found between the MSD on Ru in the ³MLCT excited state and the quantum yield of ligand dissociation in water for 1–11 (Figure 7). This finding again points to the increase in ligand exchange efficiency with a decrease in Ru d character or greater metal/ligand mixing.

³MLCT Energies and Photoanation. Additionally, a trend is also observed between the quantum yield for ligand dissociation measured in H₂O and the emission maximum measured at 77 K for 1–11 (Figure 8). Complexes with the lowest energy emission maxima, 8–11, and thus the smallest energy gaps between the ground state and lowest ³MLCT state exhibit the highest measured quantum yields of ligand dissociation. This relationship holds true for both experimental emission maxima and calculated E_{00} values obtained from DFT calculations (Table 3, Figures 8 and S26). This relationship shows that the complexes with the lowest energy emission maxima and calculated E_{00} values also have the lowest calculated MSD on the Ru metal center. As previously mentioned, computational results from the Endicott group have suggested that complexes that absorb or emit closer to the NIR region exhibit excited states that tend to possess less CT

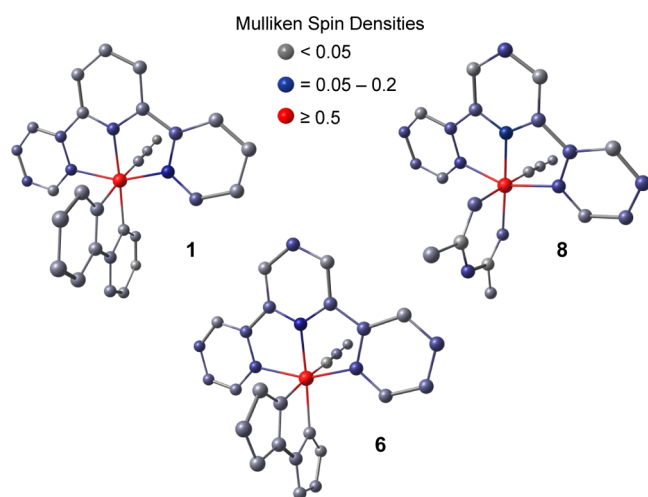


Figure 6. Pictorial representation of the calculated MSDs in the $^3\text{MLCT}$ excited state for complexes **1**, **6**, and **8**. The calculated MSD in these three complexes is representative for complexes of the same type (see Figure S25 for other complexes). Hydrogen atoms have been omitted for clarity.

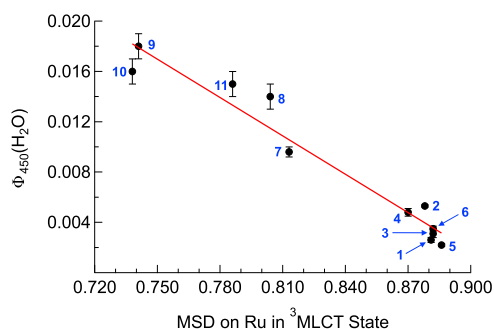


Figure 7. Plot of $\Phi_{450}(\text{H}_2\text{O})$ vs calculated MSD on Ru in the $^3\text{MLCT}$ excited state for **1–11**; the data can be fit to a line with $R^2 = 0.95$.

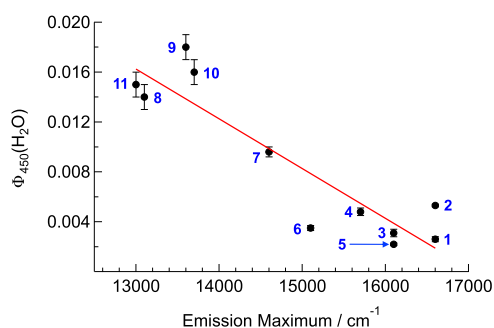


Figure 8. Plot of $\Phi_{450}(\text{H}_2\text{O})$ as a function of the emission maximum at 77 K in CH_3CN for **1–11**; the data can be fit to a line with $R^2 = 0.83$.

donating acac-type ligands, **8–12**, show that this model holds true for the $[\text{Ru}(\text{tpy})(\text{L})(\text{CH}_3\text{CN})]^{n+}$ series and that the ancillary ligands can play a significant role in affecting the character and reactivities of CT states. Previous studies by Betanzos-Lara and co-workers of Ru–arene complexes have also shown that the incorporation of electron-donating ligands enhances ligand photodissociation; however, these studies used exclusively high-energy ultraviolet or white light irradiation and offered a limited explanation of the observed differences in photoreactivity.⁶⁰

The value of $\Phi_{450}(\text{H}_2\text{O})$, 0.0012(1), of **12** did not fit the linear relationships in Figures 5, 7, and 8, and is approximately an order of magnitude lower than expected based on the values measured for the acac complex and derivatives, **8–11** (Table 3). However, when the photoanation quantum yield of **12** was measured in CH_2Cl_2 solution with 10 mM Bu_4NCl , using the same irradiation wavelength, $\Phi_{450}(\text{Cl}) = 0.021(1)$ was recorded (Table 3). This quantum yield is similar to those of **8–11**, with $\Phi_{450}(\text{Cl})$ values that range from 0.022(1) to 0.027(1) (Table 3). If these photoanation quantum yields are considered separately, complex **12** now follows the expected trend with percent Ru contribution in the HOMO, MSD on Ru in the $^3\text{MLCT}$ state, and emission energy (Figures S27–S29). These findings are consistent with the lower solubility of the Ru fragment, possessing the hydrophobic DBM ligand following the dissociation of CH_3CN from **12**, resulting in recombination with CH_3CN within the solvent cage and lower cage escape to form the aqua product.^{59,61} These findings demonstrate that the low $\Phi_{450}(\text{H}_2\text{O})$ value of **12** can be attributed to solubility of the product and/or intermediate, pointing to the importance of considering the solubilities of both fragments when designing complexes for efficient ligand photodissociation.

Although the lowest energy $^3\text{MLCT}$ state in **1–12** is $\text{Ru}(\text{d}\pi) \rightarrow \text{tpy}(\pi^*)$ in nature, a wide range of photosubstitution reactivity is observed. Therefore, the ancillary bidentate ligand must play a significant role in the photochemistry of these complexes. The spin density on the tpy ligand in the $^3\text{MLCT}$ excited state varies only slightly in **1–12** (Table 3), and not with a linear relationship, as is the case with spin density on ruthenium. The $^3\text{MLCT}$ state moves electron density from the metal to the tpy ligand. In addition, the bidentate ligand can also be used to further vary the degree of spin density removed from the ruthenium center in the excited state (Table 3). The metal center in the $^3\text{MLCT}$ excited state is partially oxidized and is calculated to possess less than one localized unpaired electron in all complexes, **1–12**. This decreased electron density on the metal center drastically reduces its ability to π -backbond to the CH_3CN ligand. Because CH_3CN is a relatively poor σ -donor, it relies on back-donation from the metal to form a strong and stable bond, such that $\text{Ru}-\text{NCCH}_3$ bond weakening is expected in the $^3\text{MLCT}$ excited state. This effect is enhanced in complexes with the lowest spin density on the metal, **8–12**, further increasing the probability of CH_3CN dissociation. It should be noted, however, that the photo-induced ligand exchange in Ru(II) polypyridyl systems with strong σ -donor leaving ligands, such as pyridines or sulfur-coordinated thioethers,^{32,62} may occur via a different mechanism, likely through the population of a dissociative ^3LF state.^{32–36}

character and more ligand-based $\pi\pi^*$ character. One way to red-shift the absorption of these types of Ru(II) complexes is to use electron-rich, donating ligands. These donating ligands raise the energy of the $\text{Ru}(\text{d}\pi)$ orbitals closer to the energy of the ligand-based π^* orbitals, thus decreasing the energy of the MLCT transition. This decreased energy gap also allows for a greater degree of mixing between the $\text{Ru}(\text{d}\pi)$ and the ligand-based π^* orbitals, such that antibonding/bonding molecular orbitals of the mixed metal/ligand character can be formed.³⁰ The low spin densities calculated for our complexes containing

CONCLUSIONS

A series of Ru(II) complexes containing the tridentate tpy ligand and various bidentate ancillary ligands were synthesized and evaluated for their ability to dissociate CH₃CN, a model for nitrile-containing drugs, upon irradiation with visible light. The bidentate ligands chosen display a similar degree of steric bulk around the metal center in the ground state, but possess a wide range of electron-donating and electron-withdrawing abilities. Complexes 1–12 display photosubstitution efficiencies that vary by approximately an order of magnitude. The complexes containing the most electron-donating bidentate ligands, 8–11, exhibit the larger quantum yield values for ligand exchange in water. Complexes 8–11 possess the smallest energy gap between the ground state and the lowest energy ³MLCT excited state, and DFT calculations show that a large degree of the ligand character is present in their HOMOs and in their ³MLCT excited states. These results suggest that ligand mixing may affect the back-bonding ability of the metal center in the excited state, increasing the quantum yields of nitrile ligand dissociation. This enhanced reactivity in the excited state is advantageous, as it allows for the design of complexes with greater quantum yields without affecting their thermal stability in the dark. The observed trends between the quantum yield of ligand dissociation and both the MSD on the Ru center in the excited state and the amount of Ru d character in the ground-state HOMO may prove to be useful in the design of new Ru(tpy)-based systems containing nitrile leaving groups.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.jpcc.9b01576.

Experimental methods, synthetic procedures and characterization data, crystallographic data for 4, 7, and 12, electronic absorption spectra, photolysis spectra and dark controls in H₂O, photoanation relationships, molecular orbitals, and MSDs, and DFT-optimized structures (PDF)

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Notes

The authors declare no competing financial interest. CCDC 1897623–1897625 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/structures/.

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