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The diastereoisomeric forms of a mononuclear Ru(II) complex bearing a bis-phenanthroline Tröger's base

Carole Bresson,[a] Michel Luhmer,[b] Martine Demeunynck,[c] Andrée Kirsch-De Mesmaeker[a] and Frédéric Pierard[a,*]

[a]*Service de Chimie Organique et Photochimie, Université Libre de Bruxelles, CP160/08, 50, Avenue F.D. Roosevelt, 1050 Brussels, Belgium*
[b]*High Resolution NMR Laboratory, Université Libre de Bruxelles, CP160/08, 50, Avenue F.D. Roosevelt, 1050 Brussels, Belgium*
[c]*LEDSS, UMR5616 & ICMG-FR2607, Université Joseph Fourier, BP53, 38041 Grenoble Cédex 9, France*

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Abstract—The synthesis of a novel completely asymmetric mononuclear complex of ruthenium(II) bearing a chiral bis-phenanthroline Tröger's base ligand **1** ($TBphen_2$) is reported. The diastereoisomeric forms of $[Ru(phen)_2TBphen_2]^{2+}$ ($\Delta S/\Lambda R = rac$-**2a** and $\Lambda S/\Delta R = rac$-**2b**) were separated through crystallization. A complete structure elucidation of the diastereoisomers in solution, including chirality assignment, was achieved by 1D and 2D NMR techniques. Photophysical characterization revealed no significant differences in the emission properties of *rac*-**2a** and *rac*-**2b** that closely resemble those of $[Ru(phen)_3]^{2+}$.

The electro/photoluminescent properties of polypyridinic ruthenium(II) complexes are attracting the interest of numerous researchers because of their potential applications. For example, these species are used as starting materials for the elaboration of electronic devices and light-emitting/harvesting systems[1–3] based on processes such as electron and energy transfer.[4] These ruthenium(II) compounds have an octahedral geometry with two enantiomeric Δ and Λ forms. Therefore, such complexes have also received considerable attention as chiral precursors for supramolecular assemblies that may have important applications in many fields of biology and chemistry.[5–7] With DNA, for example, such chiral metallic species exhibit an extreme sensitivity of the luminescence toward the DNA microenvironment and some selectivity in the diastereoisomeric interactions with the polynucleotides. In this context, we have focused our work on compounds bearing the bis-phenanthroline Tröger's base ligand ($TBphen_2$, **1**, Fig. 1).[8–10]

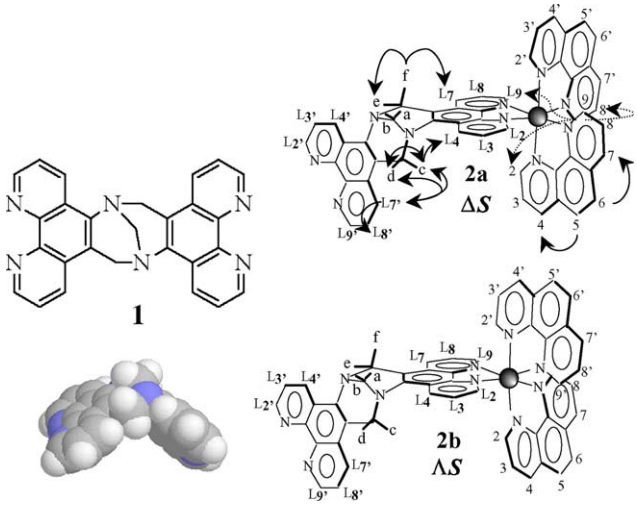

Figure 1. Structure of **1**, and of one enantiomer of each of the diastereoisomeric forms of **2** (*rac*-**2a** = $\Delta S/\Lambda R$, *rac*-**2b** = $\Lambda S/\Delta R$, phen = 1,10-phenanthroline), ^1H NMR numbering scheme and NOE correlations (arrows). Chem.3D™ representation of *S*-**1** illustrating its 'V'-shape.

Due to the blocked conformation of the two nitrogens of the diazocine bridge, Tröger's base analogs like **1** are chiral (*R* and *S*) and have a unique 'V'-shaped

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* Corresponding author at present address: Physical Chemistry Section at the Department of Chemistry and Bioscience, Chalmers University of Technology, SE-412 96 Göteborg, Sweden. Tel.: +46-31-772-30-56; fax: +46-31-772-38-58; e-mail: fpierard@chembio.chalmers.se

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structure.[11] Besides its remarkable geometry, **1** has also been reported to interact with nucleic acids and to induce DNA cleavage in the presence of copper(I).[8,12]

The first dinuclear ruthenium(II) complex bridged by **1**, $[\{Ru(bpy)_2\}_2TBphen_2]^{4+}$ (bpy = 2,2′-bipyridine) has been prepared previously.[9] However, the presence of numerous stereoisomers (up to 6) due to the combination of two ruthenium(II) centers (Δ or Λ) with the chiral ligand **1** (*R* or *S*) prevented any detailed ^{1}H NMR characterization. This stereoisomer problem should be solved with the mononuclear species. As the enantiomeric resolution of the racemic (*R*/*S*)-$TBphen_2$ did not provide sufficient enantiomeric excess,[13] we had to use the *rac*-$TBphen_2$ as starting ligand. For the precursor complex, we decided to use *cis*-$[Ru(phen)_2(py)_2]^{2+}$ (py = pyridine) instead of $Ru(phen)_2Cl_2$ for two reasons. First, *cis*-$[Ru(phen)_2(py)_2]^{2+}$ is less reactive than $Ru(phen)_2Cl_2$. Therefore, the production of the mononuclear species with $TBphen_2$ should be favored as compared to the dinuclear complex, which forms rapidly from the dichloro precursor.[9] On the other hand, *cis*-$[Ru(phen)_2(py)_2]^{2+}$ as metallic precursor would allow another strategy to be adopted in the future to solve the stereoisomer problem.[14]

In this work we report an initial approach for the synthesis, separation, and characterization of the two diastereoisomeric forms of the first mononuclear ruthenium(II) complex bearing the ligand **1**, $[Ru(phen)_2TBphen_2]^{2+}$ (**2**, Fig. 1).

Mono-chelation of **1** to yield **2** was achieved by slow addition of *rac*,*cis*-$[Ru(phen)_2(py)_2]^{2+}$ to a slight excess of *rac*-**1** in ethylene glycol at 120 °C.[17] The crude product was isolated as the hexafluorophosphate salt and purified by crystallization from acetonitrile by slow diffusion of ether in a closed vessel. Electrospray mass spectra of the crude reaction mixture and the purified product indicated the efficient separation of **2** from the more soluble dinuclear species also formed in small amounts during the synthesis.[17] Comparison of the ^{1}H NMR spectra of the crude product and the purified compound revealed the formation of a 1:1 mixture of the two possible diastereoisomers upon synthesis and also, more interestingly, a diastereoisomeric enrichment upon purification. Repeated slow fractional crystallizations allowed the isolation of pure samples of both diastereoisomeric forms, *rac*-**2a** and *rac*-**2b**, as indicated by their ^{1}H NMR spectra presented in Figure 2.

The complete assignment of chemical shifts[17] (Fig. 2) to the ligands in the structures of Figure 1, described hereafter in detail for *rac*-**2a**, was achieved with the aid of ^{1}H–^{1}H COSY spectra and steady-state NOE difference experiments (see Fig. 1).

rac-**2a** is completely asymmetric (C_1), and each of its 34 protons are therefore non equivalent, yielding 28 signals in the aromatic region, corresponding to the four phen systems, and 6 signals of the methane–diazocine bridge in the aliphatic region of the spectra. The coupling pattern for each of the four different phen units [AMX ($H_{2-4,2'-4'}$), AB ($H_{5-6,5'-6'}$), A′M′X′ ($H_{7-9,7'-9'}$), for each phen ligand and AMX ($H_{L2-4,L2'-4'}$), A′M′X′ ($H_{L7-9,L7'-9'}$) for each phen moiety of **1**] was assigned on the basis of the ^{1}H–^{1}H COSY spectrum in combination with the coupling constant values ($J_{2,3} = J_{8,9} = 5.4$ Hz, $J_{3,4} = J_{7,8} = 8.4$ Hz, $J_{2,4} = J_{7,9} = 1.2$ Hz). Identification of the protons belonging to the two phen ligands and their connectivity (i.e., $H_4 \Rightarrow H_{5-6} \Leftarrow H_7$) was established by NOE experiments through irradiation of each AB system (H_{5-6} and $H_{5'-6'}$). Due to the 'V'-shaped geometry of **1**, an increased shielding ring current effect is expected on those phen protons that lie below the plane of each phen moiety of the $TBphen_2$ ligand. Therefore, and in agreement with the coupling constant values, the most shielded resonance (already identified as belonging to a phen ligand, vide supra, 7.35 ppm for *rac*-**2a**) was assigned to H_3.

The two couples of *endo–exo* protons ($H_{c-d,e-f}$) were easily distinguished from the bridge methylene protons H_{a-b} on the basis of the coupling constant values ($J_{c,d} = J_{e,f} = 17.8$ Hz, $J_{a,b} = 12.0$ Hz) and with the aid of the ^{1}H–^{1}H COSY spectrum. The *endo* protons (H_c and H_e), each located below the plane of the opposite phen moiety of **1** as a result of the 'V'-shaped geometry of this

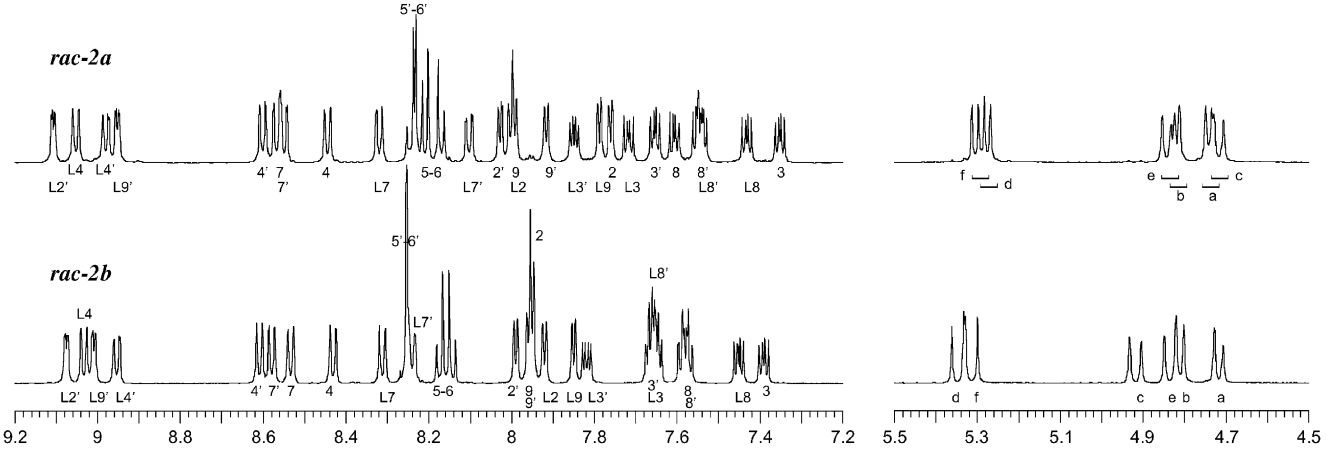

Figure 2. ^{1}H NMR spectra (600 MHz, CD_3CN, 298 K) of *rac*-**2a** and *rac*-**2b**.

Table 1. Luminescence properties of *rac*-**2a** and *rac*-**2b** compared to those of $[Ru(phen)_3]^{2+}$ (**3**) in deaerated solutions at 298 K

	H_2O			CH_3CN		
	λ_{max}, nm	τ^a, ns	ϕ^b	λ_{max}, nm	τ^a, ns	ϕ^b
rac-**2a**	608	1161	0.072	598	480	0.034
rac-**2b**	608	1198	0.069	598	488	0.035
3	601	990	0.057[19]	596	450	0.034[19]

[a] Luminescence lifetimes (±3%).
[b] Emission quantum yields (±10%).

ligand, were identified on the basis of their upfield resonances compared to the *exo* protons.[8,10] Upon simultaneous irradiation of both *exo* protons (H_d and H_f), beside the NOE shown by each *endo* proton, the intensities of two doublets in the aromatic region were enhanced, establishing these resonances to be due to H_{L7} and $H_{L7'}$. These protons were further distinguished on the basis of the deshielding effect of complexation on H_{L7} compared to $H_{L7'}$. Additional NOE experiments enabled us to assign unambiguously each *endo–exo* proton couple, the *endo* proton H_c and *exo* proton H_d showing a clear NOE connectivity to $H_{L7'}$. The assignment of the two remaining sets of coupled aromatic protons of **1** ($H_{L2-4,L2'-4'}$) was based on further NOE correlations. Irradiation of the *endo* proton H_c led, in addition to the enhancement of the signals already assigned to H_d and $H_{L7'}$, to an NOE on another doublet in the aromatic region of the spectrum allowing the assignment of proton H_{L4} to this signal. Finally, the assignment of the two remaining sets of coupled aromatic protons ($H_{2'-4'}$, $H_{7'-9'}$) was achieved through irradiation of the doublet at 7.92 ppm already identified as one of the two protons $H_{2'}$ or $H_{9'}$. Beside an NOE to the vicinal proton, NOE correlations with both H_2 and H_{L9} established the irradiated signal to arise from $H_{9'}$.

This NOE constraint requiring the close proximity of $H_{9'}$ (or $H_{2'}$) with both H_2 and H_{L9} matches only the structure of the diastereoisomer ΔS (and of its enantiomer ΛR). The stereochemistry of *rac*-**2a** was therefore assigned to the $\Delta S/\Lambda R$ enantiomeric pair. The differences of magnetic anisotropy effects due to the distinct orientation of the uncomplexed phen unit (L′) of **1** relative to the phen ligands in *rac*-**2a** and *rac*-**2b** afforded further support to the chirality assignment proposed. In *rac*-**2a**, due to the quasi-parallel orientation of L′ and one phen ligand, protons $H_{L7'}$, $H_{L8'}$, and H_c are located in the shielding cone of this phen ligand (H_{2-9}) whereas in *rac*-**2b**, the same protons are not positioned directly over the plane of a phen heterocycle and are therefore considerably less shielded [$\Delta\delta_{\mathbf{2b-2a}}$ ($H_{L7'}$) = +0.14 ppm, ($H_{L8'}$) = +0.12 ppm, (H_c) = +0.20 ppm].

rac-**2a** and *rac*-**2b** exhibit identical emission properties within experimental uncertainties (Table 1), indicating an absence of the influence of stereoisomerism on the photophysical properties of $[Ru(phen)_2TBphen_2]^{2+}$.[18]

Comparison with the emission data of $[Ru(phen)_3]^{2+}$ (**3**) showed, on the other hand, that the diazocine bridge of **1** has a weak influence on the emission properties of **2**. The slightly increased quantum yield and longer excited lifetime of **2** compared to **3** in H_2O could stem from the stabilization of the ^{3}MLCT excited state of **2** (7 nm red shift) induced by conjugation of the bridge nitrogen lone pair with the aromatic system. This would indeed reduce the efficiency of the radiationless deactivation involving thermal crossing to a higher lying ^{3}MC excited state (metal centered), a main deactivation pathway of **3**,[20] by rising the energy barrier to this excited state.

In conclusion, the diastereoisomeric forms of a mononuclear ruthenium(II) complex bearing a Tröger's base ligand were isolated for the first time and extensive use of ^{1}H NMR techniques has allowed complete structure elucidation and assignment of their stereochemistry. The crystallization procedure developed for the isolation of the diastereoisomeric forms of **2** is of particular importance. Combined with the use of the resolved enantiomers (Δ or Λ)-$[Ru(phen)_2(py)_2]^{2+}$,[16] it will yield the complete set of pure stereoisomers of **2** which could, in turn, be used as entry points for the preparation of stereochemically pure dinuclear complexes.

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17. *rac*,*cis*-$[Ru(phen)_2(py)_2]Cl_2$ was prepared according to the literature method.[15] ^{1}H NMR (300 MHz, CD_3CN, 298 K): δ ppm = 9.41 (dd, 2H, ^3J = 5.3 Hz), 8.77 (dd, 2H, ^4J = 1.2 Hz), 8.47 (dd, 4H), 8.43 (dd, 2H, ^4J = 1.3 Hz), 8.21/8.11 (AB, 4H, ^3J = 9.0 Hz), 8.18 (dd, 2H, ^3J = 8.3 Hz), 8.04 (dd, 2H, ^3J = 5.3 Hz), 7.79 (tt, 2H, ^3J = 7.7 Hz, ^4J = 1.5 Hz), 7.52 (dd, 2H, ^3J = 8.3 Hz), 7.26 (dd, 4H). ESMS: m/z = 655.1 ($[M-Cl^-]^+$, calcd $[C_{34}H_{26}N_6RuCl]^+$ 655.1); 309.8 ($[M-2Cl^-]^{2+}$, calcd $[C_{34}H_{26}N_6Ru]^{2+}$ 310.1).
$[Ru(phen)_2TBphen_2](PF_6)_2$ [**2**]$(PF_6)_2$. A solution of *rac*,*cis*-$[Ru(phen)_2(py)_2](Cl_2)$ (69 mg, 0.10 mmol) in ethylene glycol (8 mL) was added dropwise to a slight excess of *rac*-$TBphen_2$ (**1**, 51 mg, 0.12 mmol) suspended in hot ethylene glycol (8 mL). The reaction mixture was kept at 120 °C for 6 h [TLC monitoring: SiO_2; DMF/aqueous NH_4Cl 1 M (1:1)]. After cooling the solution to room temperature, the product was precipitated by addition of an aqueous saturated solution of NH_4PF_6. The orange precipitate was filtered off, washed with water, ethanol, and ether. The complex was purified by crystallization from CH_3CN by slow diffusion of ether in a closed vessel. Repeated fractional slow crystallizations yielded pure samples of both diastereoisomeric forms, *rac*-**2a** and *rac*-**2b**.
[*rac*-**2a**]$(PF_6)_2$. ^{1}H NMR (600 MHz, CD_3CN, 298 K): δ ppm = 9.11 (dd, 1H, $^3J_{2'3'}$ = 4.2 Hz), 9.05 (dd, 1H, $^4J_{24}$ = 1.2 Hz), 8.98 (dd, 1H, $^4J_{2'4'}$ = 1.2 Hz), 8.95 (dd, 1H, $^4J_{7'9'}$ = 1.2 Hz), 8.60 (dd, 1H, $^4J_{2'4'}$ = 1.2 Hz), 8.57 (dd, 1H, $^4J_{79}$ = 1.3 Hz), 8.55 (dd, 1H, $^4J_{7'9'}$ = 1.1 Hz), 8.44 (dd, 1H, $^4J_{24}$ = 1.2 Hz), 8.32 (dd, 1H, $^3J_{78}$ = 8.4 Hz), 8.24/8.22 (AB, 2H, $^3J_{5'6'}$ = 9.0 Hz), 8.21/8.17 (AB, 2H, $^3J_{56}$ = 8.8 Hz), 8.10 (dd, 1H, $^3J_{7'8'}$ = 8.4 Hz), 8.03 (dd, 1H, $^3J_{2'3'}$ = 5.4 Hz), 8.00 (dd, 1H, $^3J_{23}$ = 5.4 Hz), 7.99 (dd, 1H, $^3J_{89}$ = 5.4 Hz), 7.92 (dd, 1H, $^3J_{8'9'}$ = 5.1 Hz), 7.85 (dd, 1H, $^3J_{3'4'}$ = 8.4 Hz), 7.79 (dd, 1H, $^3J_{79}$ = 1.0 Hz), 7.76 (dd, 1H, $^3J_{23}$ = 5.4 Hz), 7.72 (dd, 1H, $^3J_{34}$ = 8.4 Hz), 7.65 (dd, 1H, $^3J_{3'4'}$ = 8.4 Hz), 7.61 (dd, 1H, $^3J_{78}$ = 8.4 Hz), 7.54 (m, 1H), 7.54 (m, 1H, $^3J_{8'9'}$ = 4.2 Hz), 7.43 (dd, 1H, $^3J_{89}$ = 5.2 Hz), 7.35 (dd, 1H, $^3J_{34}$ = 8.2 Hz), 5.30 (d, 1H), 5.28 (d, 1H), 4.84 (d, 1H, $^2J_{ef}$ = 17.8 Hz), 4.82 (AB, 1H), 4.74 (AB, 1H, $^2J_{ab}$ = 12.0 Hz), 4.72 (d, 1H, $^2J_{cd}$ = 17.4 Hz). ESMS: m/z = 1033.4 ($[M-PF_6^-]^+$, calcd $[C_{51}H_{34}N_{10}RuPF_6]^+$ 1033.2); 444.2 ($[M-2PF_6^-]^{2+}$, calcd $[C_{51}H_{34}N_{10}Ru]^{2+}$ 444.1).
[*rac*-**2b**]$(PF_6)_2$. ^{1}H NMR (600 MHz, CD_3CN, 298 K): δ ppm = 9.08 (d, 1H), 9.03 (d, 1H), 9.01 (d, 1H), 8.95 (dd, 1H), 8.61 (d, 1H), 8.58 (d, 1H), 8.53 (d, 1H), 8.43 (d, 1H), 8.31 (d, 1H), 8.25 (s, 2H), 8.24 (dd, 1H), 8.17/8.14 (AB, 2H), 7.99 (d, 1H), 7.95 (m, 3H), 7.92 (d, 1H), 7.85 (d, 1H), 7.82 (dd, 1H), 7.66 (m, 3H), 7.58 (m, 2H), 7.45 (dd, 1H), 7.39 (dd, 1H), 5.35 (d, 1H), 5.31 (d, 1H), 4.92 (d, 1H), 4.83 (d, 1H), 4.81 (AB, 1H), 4.72 (AB, 1H). ESMS: m/z = 1033.4 ($[M-PF_6^-]^+$), 444.2 ($[M-2PF_6^-]^{2+}$).
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