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ARTICLE TYPE

Enhanced stereoselectivity in a di-Ru(II) complex of an achiral bis-bidentate ligand

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The diastereoselective formation of a *meso*-dinuclear Ru(II)-complex of a novel bis-bidentate ligand is reported along with its electrochemical and photophysical properties. The design of the ligand, with its parallel coordination vectors, induces a diastereoselectivity of 1:13:1 [$\Lambda\Lambda$:($\Lambda\Delta$ or $\Delta\Lambda$): $\Delta\Delta$] for the dinuclear complex.

Ru(II)-polypyridyl complexes have attracted much attention due to their tunable electrochemical and photophysical properties,^{1a-c} which allows them to find applications in light-harvesting systems.² One simple approach to produce multinuclear Ru(II)-based chromophores is to design ligands with more than one chelating site.³ In this context, Ru(II)-bpy (bpy = 2,2'-bipyridine) based scaffolds are photophysically more useful synthons as opposed to the synthetically and structurally more appealing tpy (tpy = 2,2';6',2''-terpyridine) based scaffolds.⁴ Polynuclear Ru(II)-complexes of bidentate ligands often require purification of stereoisomers and this stereochemical complexity increases with the addition of each metal ion.⁵ Nonetheless, owing to their stereoselective interactions with DNA, the isomerically pure Ru(II)-complexes with bidentate ligands have shown potential as DNA probes.⁶ They can also be used as enantiopure building blocks in supramolecular assemblies.⁷

Many attempts have been made to separate enantiomers and diastereomers of Ru-polypyridyl complexes. Although the pioneering work of chromatographic separation based on cation exchange and ion pairing using non-chiral anionic additives, such as toluene-4-sulfonate, developed by Keene and co-workers, has been proven to work, the major drawback of this method is that relatively long separation times are sometimes required.^{8a-b} Chiral resolution using capillary electrophoresis⁹ and capillary zone electrophoresis with enantiopure tartrate salts¹⁰ and chiral-DNA⁹ have also been proven to be useful. Chiral discrimination of Ru-complexes on silica column using Δ or Λ -P(V)catecholato complexes could also be achieved, as shown by Lacour¹¹ and Gruselle.¹² Recently, Vos and Macdonnell *et al.* have developed enantiomeric separations of Ru(II)-polypyridyl complexes using HPLC with teicoplanin¹³ and cyclodextrin⁶ chiral stationary

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phases (CSPs).

In order to control the stereoselectivity of the final product, we introduced parallel coordination vectors into the bridging ligand (BL) such that adjacent [Ru(bpy)₂]-units could only enter the coordination site in opposite enantiomeric forms. Although ligands **L2**, **L3** and **L4** in Chart 1 possess parallel coordination vectors, **L2** doesn't form dinuclear complexes chelated by the N-atoms due to steric hindrance. In **L3** and **L4**, the coordination vectors are anti-parallel, so they also afford mixtures of *rac* and *meso*-dinuclear complexes. BLs with angular coordinated vectors, for e.g., **L5** to **L11**, have been shown to afford a mixture of *rac*-($\Lambda\Lambda$ or $\Delta\Delta$) and *meso*-($\Lambda\Delta$ or $\Delta\Lambda$) dinuclear complexes upon complexation with the [Ru(bpy)₂]-unit. Thus, we designed a bis-bidentate ligand that can (i) accommodate two [Ru(bpy)₂]-units, (ii) offer parallel coordination vectors with larger bite angles compared to **L2-L11** that force coordinated complexes into close proximity.

We present herein a novel bis-bidentate ligand, **dgpm** (**L1**) (dgpm = diguanidinepyrimidine) (chart 1) in which the two coordination vectors are parallel. Dinuclear Ru(II)-complex of **dgpm** has been synthesized and characterized by solution NMR, UV-vis absorption spectroscopy, cyclic voltammetry and XRD. Also, due to the unique design of **dgpm**, the *meso*-dinuclear complex is formed with high diastereoselectivity.

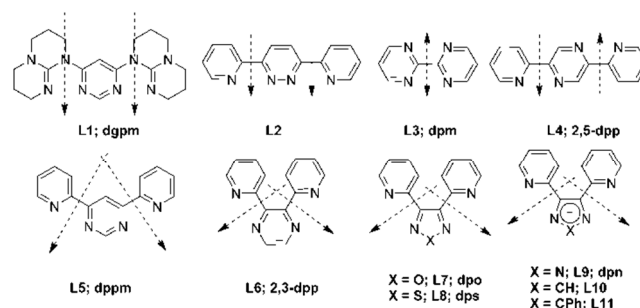
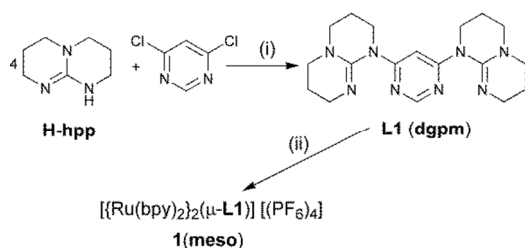


Chart 1: Ligands with different coordination vectors, as shown by dashed arrows, in their bis-bidentate chelating mode.

The bis-bidentate chelating ligand, **L1** (diguanidinepyrimidine; **dgpm**), could be synthesized conveniently by microwave-assisted heating using 4 equivalent of 1,3,4,6,7,8-hexahydro-2H-pyrimido[1,2- α]pyrimidine (**H-hpp**), in 90% yield (Scheme 1). Complex **1** (*meso*) ([{Ru(bpy)₂}₂(μ -**L1**)] [(PF₆)₄]) was synthesized by refluxing a butanol mixture of **L1** and *cis*-Ru(bpy)₂Cl₂ · 2H₂O in 1:3.5 molar ratios. A satisfactory yield was obtained after purification by column chromatography, followed

by anion metathesis. For reaction ii the product is a heterochiral *meso*-diruthenium complex, **1(meso)**, which can be isolated in 1:13:1 ($\Lambda\Lambda:\Delta\Delta$ (or $\Delta\Lambda$): $\Delta\Delta$) (see Fig. S4 in ESI) ratio over its homochiral form using a simple silica column chromatography without using a chirally pure [Ru]-precursor or chiral ion-exchange chromatography.¹⁴ The coordination vectors in **L1** are parallel and it forms six membered ring cycles upon coordination (Chart 1), which in turn precludes the formation of sterically demanding $\Lambda\Lambda$ or $\Delta\Delta$ *rac*-isomers and maximizes the possibility of π - π interaction between the bpy units of each Ru-centre in complex **1(meso)**.



Scheme 1: Syntheses of ligand **L1** and complex **1(meso)**.[†]

[†](i) toluene, microwave at 160 °C; 90%; (ii) *cis*- $\text{Ru}(\text{bpy})_2\text{Cl}_2$ (3.5 eq) in *n*-butanol at reflux followed by the addition of KPF_6 ; 65%.

The ¹H NMR spectrum of **L1** is symmetric in nature and exhibits two aromatic and six aliphatic peaks. This symmetric nature suggests a fast equilibrium between the equatorial and axial protons residing on the same carbon atom in the unsaturated **hpp** backbone. Attaching a heterocycle to the guanidine NH-position of **H-hpp** renders the six annular methylene units nonequivalent by both ¹H and ¹³C NMR spectroscopies in contrast to free **H-hpp**.¹⁵ Based on racemic $\text{Ru}(\text{bpy})_2\text{Cl}_2$ starting material, the helicity of bpy ligands induces stereogenicity onto the two Ru-centres in **1(meso)**, with the possibility of Λ and Δ -enantiomers. However, the relatively simple ¹H and ¹³C NMR spectra of **1(meso)** suggest a favorable formation of $\Lambda\Lambda$ (or $\Delta\Delta$) diastereomer over (also revealed by crystallography) a possible statistical combination of 1:2:1 = $\Lambda\Lambda:\Lambda\Delta:\Delta\Delta$. In the ¹H NMR spectrum of the complex, the farthest upfield singlet peak is at 6.1 ppm, which may be attributed to the 5-pyrimidyl proton due to the shielding by adjacent **hpp** moieties. Based on ¹H NMR assignment, Polson *et. al.* had previously reported a diastereoselectivity of 4:9:1 = $\Lambda\Lambda\Lambda:\Lambda\Lambda\Delta$ (= $\Delta\Delta\Lambda$): $\Lambda\Delta\Delta$ in a triruthenium complex.¹⁴ The existence of a singlet peak at 6.1 ppm in the ¹H NMR spectrum of reaction ii (Fig. S2 in ESI), albeit with a very minor impurity, suggests the exclusive formation of the *meso*-isomer.

The single crystal X-ray structure of **1(meso)** confirms the *meso*-structure and reveals two coordinatively saturated Ru(II) ions in a distorted octahedral geometry. The Ru-N bonds to bpy nitrogens were found to be shorter than those to pyrimidine and **hpp**-nitrogens, which in turn suggest strong σ -donation from **hpp** units and back π -bonding to the bpy moieties (Table T2 in ESI). Although the two Ru-atoms are perfectly planar with the central pyrimidine ring, thereby increasing the possibility of better electronic communication through the BL, the overall C2-symmetry of this cation is lost in the solid state due to spatial arrangement of the bpy units which are bowed towards one

another, forming effective offset face-to-face π - π interactions.¹⁶ This deformation is due to the flexible alkyl linkers which allow non-planar chair conformation of the BL.^{17a,b} As a consequence the parallel coordination vectors in **L1** maximize the possibility of π - π interaction.

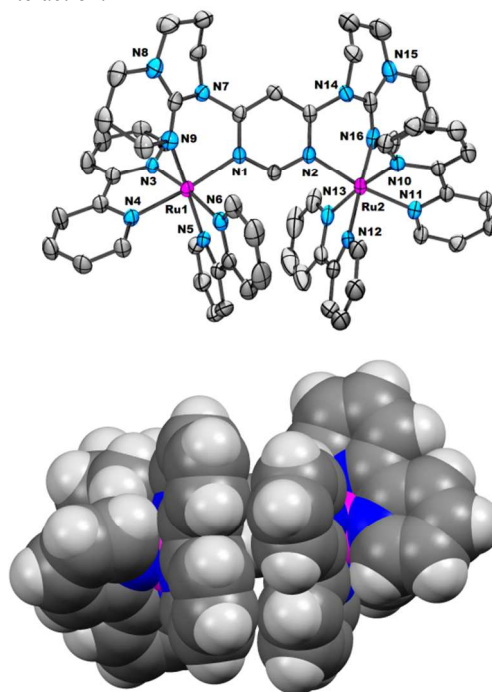


Fig. 1 Perspective views of complex **1(meso)**, (i) with partial labeling (top), (ii) spacefill model of **1(meso)**, along the plane of central pyrimidine ring, showing the π - π interaction of the bpy units, favoring for the diastereoselective formation of $\Lambda\Lambda$ (or $\Delta\Delta$)-isomer over $\Delta\Delta$ or $\Lambda\Lambda$ -isomer (bottom). Hydrogen atoms, anions and solvated acetonitrile molecule are not shown for clarity; the ellipsoids correspond to 50% probability level.

The electrochemical behaviour of crystallized complex **1(meso)** has been examined by cyclic voltammetry, which exhibits two and five mono-electronic quasi-reversible oxidations and reductions, respectively. Despite short intermetallic distance of 5.903 Å, the metal based oxidations indicate weak communication ($\Delta E_{\text{ox}} = 160$ mV) in acetonitrile solution as shown by a small comproportionation constant (K_c) value equal to 506. This value is identical to what is found for the dinuclear complex containing ligand **L5** (or dppm) (Table T3 in ESI) and related compounds as the pyrimidine BLs.¹⁸ Key factors like metal-metal distance, the electron density of the LUMO at the coordinating centres,^{19a,b} and the nature of the bridge can influence the M-M interaction. With short internuclear metal-metal separations and **L3** as BL, it has been proposed that electron transfer may be through the direct orbital overlap of the metal d orbitals,^{19a,20} and may be the same in this study. In the cathodic region, among five quasi-reversible reductions, the first four reductions are bpy based, while the last one is pyrimidine based. Although, theoretically, in dinuclear Ru-complexes, bearing electron deficient diazine BLs (for e.g. **L3**, **L5** and **L6**) the first reduction usually involves electron transfer into the BL,^{1a,3,21} due to strong σ -donation from the hpp units, the BL is now difficult to reduce. A relative comparison of the oxidation potentials among **1(meso)** and dinuclear Ru-complexes

comprising anionic BLs **L9** and **L10**, suggests that **L1** is the strongest donor.

The electronic absorption spectra of crystallized **L1** and **1(meso)** were recorded in dry, degassed acetonitrile (Fig. S6 and Table T4 in ESI). Five main transitions are observed in the electronic absorption spectra of complex **1(meso)**, where the first two high energy transitions at 244 and 289 nm are essentially LC transitions. The transitions at 368 and 470 nm have been ascribed to MLCT, with non-negligible contributions from LC transitions as suggested by TD-DFT calculation of similar compounds.²⁰ So, these transitions may be assigned as ¹(ML)LCT (singlet metal-ligand to ligand charge transfer) transitions.

The spectral progression accompanying the oxidation (**1meso**)⁴⁺ to (**1meso**)⁵⁺ and (**1meso**)⁶⁺ in 0.1 M [(*n*-C₄H₉)₄N]PF₆− CH₃CN at ambient temperature was monitored (Fig. S8 in ESI). The lowest energy absorption band at 368 nm decreased in energy and intensity following one electron oxidation to mixed valence (5+) species on changing potential from 600 mV to 700 mV and collapsed completely at 800 mV. The fate of the other low energy absorption band at 470 nm is similar, but the decrease is gradual with increasing the applied potential. New bands appear at 316 nm and 600 nm (16700 cm⁻¹) with continued oxidation from 4+ to 5+ to 6+ species, which could be assigned as LC and ligand-to-metal charge transfer (LMCT) transitions, respectively, and the latter is consistent with the π(bpy) → dπ(Ru^{III}) LMCT transition at 17160 cm⁻¹ in [Ru^{III}(bpy)₃]³⁺.²³ A similar LMCT band is also observed in the mixed valence species upon oxidation by equimolar amount of cerium ammonium nitrate (CAN) (Fig. S7 in ESI).

Conclusions

In conclusion, a novel bis-bidentate ligand, **dgpm** was attached with two [Ru(bpy)₂]²⁺ units. The predominant diastereoselective formation of *meso*-isomer, without using enantiopure [Ru]-precursor or chiral chromatographic separation, is facilitated by three factors (i) rigid and thermodynamically stable chair conformation of the BL, which offers parallel coordination vectors (ii) stable six-membered chelate ring formation upon complexation and (iii) maximum possible π-π interaction between the bpy units of each Ru-centre. Complex **1(meso)** oxidizes at low positive potential, thus confirming the high σ-donating nature of **dgpm**. This complex also exhibits LMCT absorption upon gradual one-electron oxidation, chemically or spectroelectrochemically, without any intervalence charge transfer (IVCT) band when scanned up to 3000 nm, which suggests that the oxidation states of the two metal sites are distinct and do not readily interconvert. The overall stereoselectivity could be increased by adding steric bulk to the periphery of the bpy units. The ensuing increase in unfavourable steric interactions between the bpy units in the *rac*-isomer would disfavor formation. Alternatively, by increasing the π-surface of the bpy units that are involved in face-to-face π-interactions or changing these bpy units with 1,10-phenanthroline, with higher degree of planar π-interactions, the diastereoselectivity may be increased even more and these investigations are underway.

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Notes and references

Crystal data for 2: [C₅₈H₅₈N₁₆Ru₂][4(PF₆)] [2(C₂H₅N)], M = 1843.33, Monoclinic, *a* = 22.038(2) Å, *b* = 14.0363(13) Å, *c* = 25.925(3) Å, *α* = 90°, *β* = 112.384(2)°, *γ* = 90°, *V* = 7415.2(13) Å³, *T* = 150(2) K, space group *Cc*, *Z* = 4, 108217 reflections measured, 13608 independent reflections (*R_{int}* = 0.0597). The final *R_i* value is 0.0382 (*I* > 2σ(*I*)). The final *wR(F²)* value is 0.1008 (*I* > 2σ(*I*)). The final *R_i* value is 0.0384 (all data). The final *wR(F²)* value is 0.1011 (all data); (CCDC 964842).

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