Tuning the Rotational Behavior of Lopsided Heterocyclic Nitrogen Ligands (L) in Octahedral *cis*-[Ru(bpy)$_2$(L)$_2$](PF$_6$)$_2$ Complexes. A Variable-Temperature ^{1}H NMR Study

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In this paper are presented the syntheses, characterizations, and dynamic solution behaviors of three *cis*-[Ru(bpy)$_2$(L)$_2$] (bpy = 2,2′-bipyridine) complexes, **1**−**3**, in which L represents the monodentate ligands 1-methylimidazole (MeIm), 1,2-dimethylimidazole (Me$_2$Im), and 1-methylbenzimidazole (MeBim), respectively. Because of their different steric properties, these three monodentate ligands yield complexes that show quite different fluxional behaviors in solution. These behaviors are studied with several ^{1}H NMR techniques at various temperatures between −95 and +55 °C. The ^{1}H NMR spectra of **1**, which has the smallest monodentate ligand of the three used, indicate the complex to be in fast exchange (i.e., the imidazoles rotate around their Ru−N axes) at all recording temperatures. The sterically more demanding ligands, Me$_2$Im and MeBim, in **2** and **3**, respectively, are in fast exchange at 55 °C and in slow exchange at low temperatures, showing three different atropisomers: two head-to-tail (HT) isomers and one head-to-head (HH) isomer. The newly synthesized bidentate ligand 1,2-bis-(1-methyl-2-benzimidazolyl)ethane (mdbz) forms the complex *cis*-[Ru(bpy)$_2$(mdbz)](PF$_6$)$_2$ (**4**), in which the two benzimidazole moieties are constrained and relatively fixed. The two tethered benzimidazoles in **4** cannot rotate around their Ru−N axes, and therefore **4** is a good model for the main HT isomer of **3**.

Introduction

Understanding the binding of "biological molecules" to metal compounds is of great importance in many areas of bioinorganic chemistry[1] and in particular also in the field of biomedicinal chemistry.[2,3] For platinum-containing antitumor complexes, for example, the binding to the DNA bases and more specifically to the N7 of guanine has been revealed to be crucial for their antitumor activity.[4−6] The structures, dynamics, and energetics of cis Pt adducts have been extensively studied and are in an advanced stage of being understood.[7,8] In contrast to the case of these platinum complexes, the factors influencing the coordinations, orientations, and dynamic behaviors of cis-coordinated lopsided ligands in octahedral complexes are much less well understood. Such knowledge is important to the understanding of coordinative binding of biologically available N-heterocycles to six-coordinated metal ions,[9] e.g., ruthenium, of which several complexes are currently under investigation for their antitumor properties.[10,11] In vivo, some of these ruthenium complexes are thought to hydrolyze[12−14] and cause tumor death by their binding to DNA bases[15] similarly to the platinum compounds. Ruthenium(II/III) complexes are generally octahedral and six-coordinated, and therefore their bifunctional coordination to (DNA) bases is sterically much more constrained than that of the square-planar four-coordinated platinum complexes. The antitumor-active [Ru(dmso)$_4$Cl$_2$] complexes have been proven to be suitable compounds for the investigation of the binding of DNA bases to octahedral (ruthenium) complexes.[16−19] On reaction of *cis*-[Ru(dmso)$_4$Cl$_2$] with DNA model bases such as imidazole and benzimidazole derivatives (L), the cis bis complexes [Ru(dmso)$_2$Cl$_2$(L)$_2$] are formed, in which the lopsided heterocycles can adopt different kinds of orientations and show interesting fluxional behaviors in solution.[20−23]

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Chart 1. Structural Representation and Proton-Numbering Scheme for the Λ Enantiomer of *cis*-$[Ru(bpy)_2(L)_2]^{2+}$ (Left) Along with Its Schematic Representation (Right)

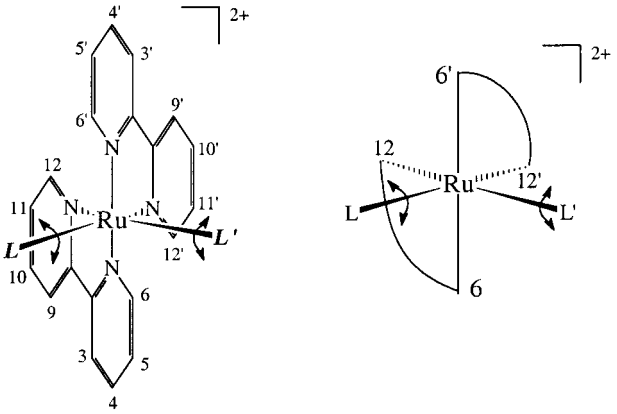
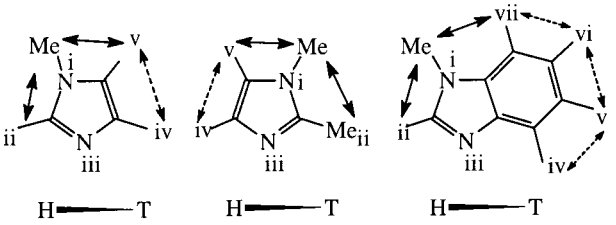


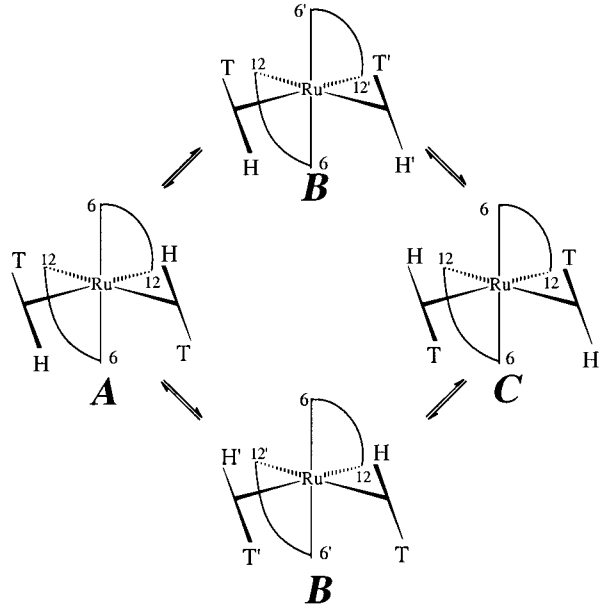
Chart 2. Proton-Numbering, NOE-Coupling (Solid Arrows), and COSY-Coupling (Dashed Arrows) Schemes for MeIm (Left), Me_2Im (Middle), and MeBim (Right)[a]



[a] The HT ("head-to-tail") rods represent the orientations of the imidazole ligands as used in Chart 3.

Recently, we communicated[24] the observation and identification of all (three) possible atropisomers of the bifunctionally coordinated ruthenium(II) complex *cis*-$[Ru(bpy)_2(MeBim)_2](PF_6)_2$, in which bpy is 2,2′-bipyridine and MeBim is the bicyclic ligand 1-methylbenzimidazole. The MeBim ligands appear to rotate freely on the NMR time scale above room temperature; upon lowering of the temperature, the rotation around the Ru−N axes slows, and finally the MeBim ligands are stationary on the NMR time scale at −95 °C. This study predicted that the system *cis*-$[Ru(bpy)_2(L)_2](PF_6)_2$ (Chart 1) would be very suitable for studying the coordinative and rotational aspects of heterocyclic ligands using ^{1}H NMR spectroscopy. We now present and compare the fluxional behavior of three monodentate lopsided ligands in the bifunctionally coordinated complexes *cis*-$[Ru(bpy)_2(MeIm)_2](PF_6)_2$ (**1**), *cis*-$[Ru(bpy)_2(Me_2Im)_2](PF_6)_2$ (**2**), and *cis*-$[Ru(bpy)_2(MeBim)_2](PF_6)_2$ (**3**), in which MeIm is 1-methylimidazole and Me_2Im is 1,2-dimethylimidazole (Chart 2). By the use of 2D NMR techniques such as COSY, NOESY, and ROESY, the detailed orientations of the imidazole ligands in the complexes were determined and their rotational behaviors were studied at various temperatures. The use of PF_6 salt complexes and acetone-d_6 as the solvent appears to be a good combination for performing measurements on the *cis*-$[Ru(bpy)_2(L)_2]^{2+}$ complexes, as it offers a relatively large temperature range in which NMR experiments can be performed (from +55 down to −95 °C); even at the low temperatures in this range, the compounds show a solubility sufficient for carrying out the 2D experiments.

Chart 3. Schematic Representations of the Four (Three Different) Atropisomers of **2** and **3**, with the Arcs Representing the bpy Ligands and the Rods Representing the Imidazole Derivatives[a]



[a] The arrows represent the interconversion pathway of the atropisomers, each via a single rotation of one of the imidazole ligands by about 180°.

R-imidazole ligands are lopsided ligands in which we can define the H(ii) (MeIm and MeBim) or H(iv) (Me_2Im) side as the "head" and the H(iv) (MeIm and MeBim) or Me(ii) (Me_2-Im) side as the "tail" (Chart 2). For two cis-coordinated imidazoles on a metal ion, the corresponding atoms can be on the same side (head-to-head, HH) or on opposite sides (head-to-tail, HT) of the N(iii)-Ru−N(iii′) plane. The two benzimidazoles in **3** can both orient in two different ways, resulting in three different atropisomers (Chart 3): two HT conformers (which each have a 2-fold symmetry axis) and two identical HH conformers (which lack a 2-fold symmetry axis).[24] One HT conformer (later referred to as **A**) has the two monodentate ligands positioned with their phenyl rings ("tail") wedged between the two bpy ligands, while the other HT conformer (**C**) has the two benzimidazoles rotated around their Ru−N axes by about 180° with respect to the orientations in **A**. The HH conformer (**B**) has one of the two benzimidazoles (H(ii)−H(iv)) oriented with the phenyl ring positioned between the two bpy's, as in **A**, while the second one (H(ii′)−H(iv′)) is oriented like in **C**. Although the *cis*-$[Ru(bpy)_2]$ moiety is a chiral system, the coordinated imidazoles used in this study are not, so the ^{1}H NMR signals of the two enantiomers of each atropisomer of the *cis*-$[Ru(bpy)_2(L)_2]^{2+}$ complexes are indistinguishable in our experiments.

To confirm the assignments of the orientations of the imidazole ligands in the complexes, and in particular the benzimidazole ligands in **3**, we designed and synthesized the new complex *cis*-$[Ru(bpy)_2(mdbz)](PF_6)_2$ (**4**), in which mdbz is the bidentate ligand 1,2-bis(1-methyl-2-benzimidazolyl)ethane (Chart 4). From a molecular model, mdbz was expected to coordinate to $Ru(bpy)_2$ with the tethered benzimidazole moieties oriented similarly to the benzimidazoles in the most abundant

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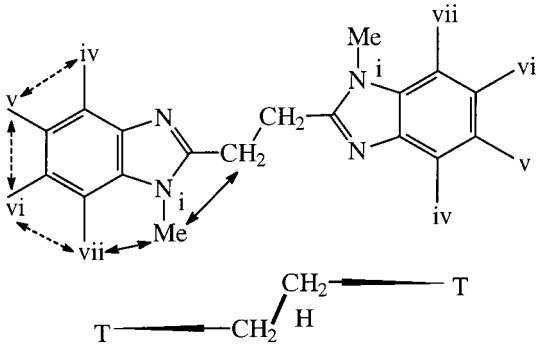
Chart 4. Proton-Numbering, NOE-Coupling (Solid Arrows), and COSY Coupling (Dashed Arrows) Schemes for mdbz[a]



[a] The THT ("tail-to-head-to-tail") rod represents the orientation of mdbz as used in Chart 6.

atropisomer of **3**, **A**. The presence of the ethylene bridge prevents rotation of the two benzimidazole moieties around their Ru−N axes.

Experimental Section

Materials. Hydrated $RuCl_3$ was used as received from Johnson Matthey Inc. 2,2′-Bipyridine (Fluka), 1-methylimidazole (Acros), 1-methylbenzimidazole (Aldrich), and 1,2-dimethylimidazole (Merck) were also used as received, and *cis*-$[Ru(bpy)_2Cl_2]\cdot 2H_2O$ was prepared according to a literature procedure.[25]

1,2-Bis(1-methyl-2-benzimidazolyl)ethane, mdbz, was prepared as described earlier for the synthesis of 1,3-bis(1-methyl-2-benzimidazolyl)propane[26] from 1,2-phenylenediamine and succinic acid with consecutive methylation of the bis(2-benzimidazolyl)ethane. Yield: 75%. Anal. Calcd for $C_{18}H_{18}N_4$: C, 74.5; H, 6.3; N, 19.3. Found: C, 73.2; H, 6.4; N, 19.1. ^{1}H NMR (acetone-d_6): δ 7.55 (d (^3J = 8 Hz), 2H), 7.43 (d (^3J = 8 Hz), 2H), 7.20 (t, 2H), 7.15 (t, 2H), 3.87 (s, 6H), 3.53 (s, 4H).

***cis*-[Ru(bpy)$_2$(MeIm)$_2$](PF$_6$)$_2$, 1**, was prepared by a method slightly different from the one reported by Geraty and Vos.[27] *cis*-$[Ru(bpy)_2Cl_2]\cdot 2H_2O$ (0.26 g, 0.51 mmol) and 1-methylimidazole (0.41 g, 5.0 mmol) in 50 mL water were refluxed for 2.5 h. The reaction mixture was filtered at room temperature, and a concentrated aqueous solution of NH_4PF_6 (0.87 g, 5.4 mmol) was added to the clear red filtrate. The precipitate that formed was isolated by filtration and washed with water. Recrystallization from acetone/water yielded a red crystalline material which was isolated by filtration and washed with diethyl ether. Yield: 0.33 g (75%).

***cis*-[Ru(bpy)$_2$(Me$_2$Im)$_2$](PF$_6$)$_2$, 2**, was synthesized as described for **1**, but with the use of 1,2-dimethylimidazole instead of 1-methylimidazole. Yield: 0.38 g (85%). Anal. Calcd for $RuC_{30}H_{32}N_8P_2F_{12}$: C, 40.2; H, 3.6; N, 12.5. Found: C, 40.1; H, 3.4; N, 12.3.

***cis*-[Ru(bpy)$_2$(MeBim)$_2$](PF$_6$)$_2\cdot$CH$_3$COCH$_3$, 3**, was synthesized as described for **1**, but with the use of 1-methylbenzimidazole instead of 1-methylimidazole. Yield: 0.41 g (85%). Anal. Calcd for $RuC_{39}H_{38}N_8OP_2F_{12}$: C, 45.6; H, 3.7; N, 10.9. Found: C, 45.3; H, 3.7; N, 10.7.

***cis*-[Ru(bpy)$_2$(mdbz)](PF$_6$)$_2\cdot$H$_2$O, 4.** *cis*-$[Ru(bpy)_2Cl_2]\cdot 2H_2O$ (0.26 g, 0.51 mmol) and mdbz (0.15 g, 0.50 mmol) were refluxed in water for 3 h. The white precipitate that formed was filtered off, and NH_4PF_6 (0.5 g in 2 mL of H_2O) was added to the orange-red filtrate, giving solid complex **4**, which was isolated by filtration and recrystallized from acetone/water as a red-orange microcrystalline powder. Yield: 0.35 g (70%). Anal. Calcd for $RuC_{38}H_{36}N_8OP_2F_{12}$: C, 45.1; H, 3.7; N, 11.1. Found: C, 44.9; H, 3.5; N, 10.8.

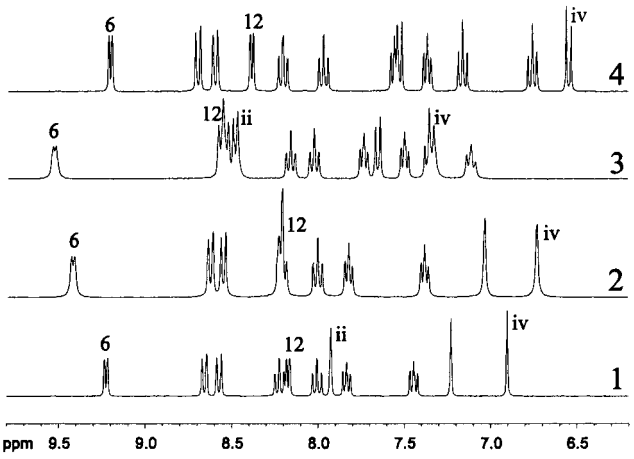


Figure 1. Aromatic regions of the ^{1}H NMR spectra of *cis*-$[Ru(bpy)_2(MeIm)_2](PF_6)_2$, **1**, and *cis*-$[Ru(bpy)_2(mdbz)](PF_6)_2$, **4**, at RT and of *cis*-$[Ru(bpy)_2(Me_2Im)_2](PF_6)_2$, **2**, and *cis*-$[Ru(bpy)_2(MeBim)_2](PF_6)_2$, **3**, at 55 °C in acetone-d_6. Assignments are defined in Charts 1 and 2.

Instruments and Techniques. Elemental analyses were performed by the analytical department of University College Dublin.

All ^{1}H NMR measurements were performed at 300.13 MHz on a Bruker 300 DPX spectrometer, equipped with a Bruker B-VT1000 variable-temperature unit, which was calibrated against an MeOH sample. All spectra were calibrated against the CD_3COCD_2H peak, 2.06 ppm. The 1D proton and HH COSY spectra were obtained using the standard Bruker pulse sequences. The NOESY experiments[28] were performed with a mixing time of 1 s and 16 scans for each t_1 increment; a delay of 2 s was incorporated prior to each scan. The ROESY spectra were obtained using the Bruker pulse program with a special spin lock from a series of 180° pulses for phase-sensitive mixing using TPPI.[29,30] The spin lock field used was 2.5 kHz, and it was implemented for 500 ms. There were 16 scans for each t_1 increment, and a 1.5 s delay was incorporated before each scan.

Results and Discussion

High-Temperature NMR Spectra. In Figure 1 are shown the aromatic regions of the ^{1}H NMR spectra of *cis*-$[Ru(bpy)_2(MeIm)_2](PF_6)_2$, **1**, and *cis*-$[Ru(bpy)_2(mdbz)](PF_6)_2$, **4**, in acetone-$d_6$ at room temperature (RT). The ^{1}H NMR spectra of *cis*-$[Ru(bpy)_2(Me_2Im)_2](PF_6)_2$, **2**, and *cis*-$[Ru(bpy)_2(MeBim)_2](PF_6)_2$, **3**, at RT show strongly broadened peaks, but at 50 °C, well-resolved sharp resonances are observed (Figure 1). For all four spectra shown in Figure 1, the number of signals observed is half that of the total amount of protons present in the compounds, indicating a 2-fold symmetry to be present in the systems. In theory, these spectra cannot indicate whether the ligands are rapidly rotating on the NMR time scale.[9] From previous studies on **3**, it is known[24] that its ^{1}H NMR spectrum at 50 °C is the average of three atropisomer spectra; at this temperature, these are in fast exchange on the NMR time scale. The variable-temperature ^{1}H NMR behavior of **2** is similar to that of **3**, indicating the Me_2Im ligands in **2** to be rapidly or slowly rotating on the NMR time scale, depending on the temperature. MeIm is a smaller ligand than MeBim and Me_2-Im, and therefore the spectrum of **1** at RT (and at 50 °C) most likely also represents a system in which the imidazole ligands are rapidly rotating. mdbz, in contrast, has two benzimidazole units which are tethered, preventing independent rotation around the Ru−N axes, and therefore the spectrum of **4** shown in Figure

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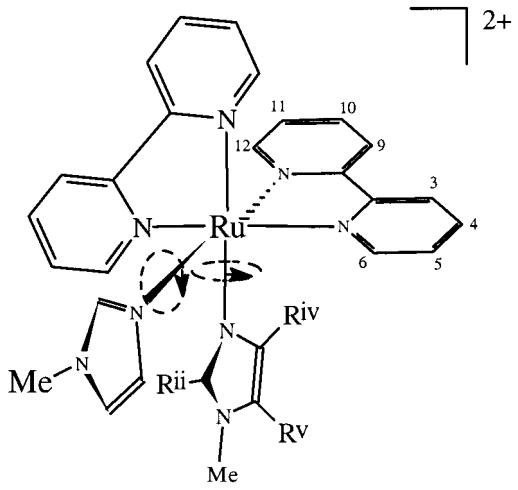
Chart 5. Structural Representation and Proton-Numbering Scheme for the Λ Enantiomer of Complexes **1**−**3**, *cis*-$[Ru(bpy)_2(RIm)_2]^{2+}$



1 is an example of a C_2-symmetric $Ru(bpy)_2$ complex in which the ligands are not rotating on the NMR time scale; vide infra.

Rapidly Rotating Ligands: *cis*-$[Ru(bpy)_2(MeIm)_2](PF_6)_2$. At high temperature (50 °C) and at low temperature (down to −95 °C), the ^{1}H NMR spectra of **1** are very similar to the spectrum at RT, showing only one set of (eight) bpy proton resonances and one set of (four) methylimidazole peaks. As mentioned above, such a temperature-independent behavior can indicate either that the MeIm ligands are rapidly rotating on the NMR time scale at all temperatures, or that they are not rotating at all. In complexes **2** and **3**, Me_2Im and MeBim, respectively, appear to be ligands that are in fast exchange at high temperatures only; vide infra. Compound **1** (Chart 5) has two untethered MeIm ligands which are sterically less demanding than Me_2Im or MeBim, and therefore it is reasonable to assume that, at high temperature, the two MeIm ligands of **1** are relatively rapidly rotating. Because the ^{1}H NMR spectrum of **1** does not change significantly on cooling, it can be concluded that, even at low temperatures, the MeIm ligands are rapidly rotating on the NMR time scale. The fast rotation of the MeIm ligands (Chart 5) even at low temperatures is confirmed by the NOESY spectra (Figure 2), in which cross-peaks of the bpy H6 proton with both the MeIm H(ii) and the H(iv) protons of the imidazole are present. Also, cross-peaks of H12 with both H(ii) and H(iv) are observed, as expected for a rotating MeIm. From the structures of *cis*-$[Ru(bpy)_2(Im)_2]^{2+}$ and *cis*-$[Ru(bpy)_2(Im)(H_2O)]^{2+}$, derived from single-crystal X-ray diffraction data,[31] we assume that the MeIm ligands can rotate freely around their Ru−N axes, as no great steric barriers are present.

Moderately Rotating Ligands, *cis*-$[Ru(bpy)_2(Me_2Im)_2](PF_6)_2$ and *cis*-$[Ru(bpy)_2(MeBim)_2](PF_6)_2$. Variable-Temperature (VT) Behavior. Complexes **2** and **3** appear to be fluxional systems on the NMR time scale which are in fast exchange at about 50 °C (Figure 1). A NOESY spectrum of **3** at 330 K (Supporting Information) confirms that the benzimidazole ligands rotate rapidly on the NMR time scale because H(ii) and H(iv) give cross-peaks that are similar to those present in the above-discussed MeIm spectra. Upon lowering of the temperature, all proton signals of **3** start to broaden and eventually result in two sets of 13 peaks (**A** and **C**) and one set of 26 peaks (**B**) at −95 °C. From characteristic interligand NOE cross-peaks between the benzimidazole H(ii) and H(iv) resonances and between the bpy H6 and H12 resonances, the three sets of signals could be unambiguously assigned to all three possible rotamers of **3** as depicted in Chart 3.[24] The relative abundances of the three rotamers at −95 °C were calculated from the integration values of the H6 peaks: **A**, 75%; **B**, 15%; **C**, 10%. In Figure 3, the VT behavior of **3** is shown in the low-field region of the spectrum where only the H6 signals are observed. At −95 °C, the H6 resonances of the three atropisomers are well separated by about 0.3 ppm (Table 1). When the temperature is increased, the doublets first begin to broaden and consecutively move toward each other, then coalesce at about 0 °C, and finally give one clear doublet at 9.53 ppm at 50 °C. Because the receiver gain and the number of scans were kept constant during the recording of the separate spectra, the apparent difference in intensity between the signals at different temperatures is related to the enhanced sensitivity of the ^{1}H resonances at lower temperatures due to the higher population difference in the nuclear Zeeman levels.[32]

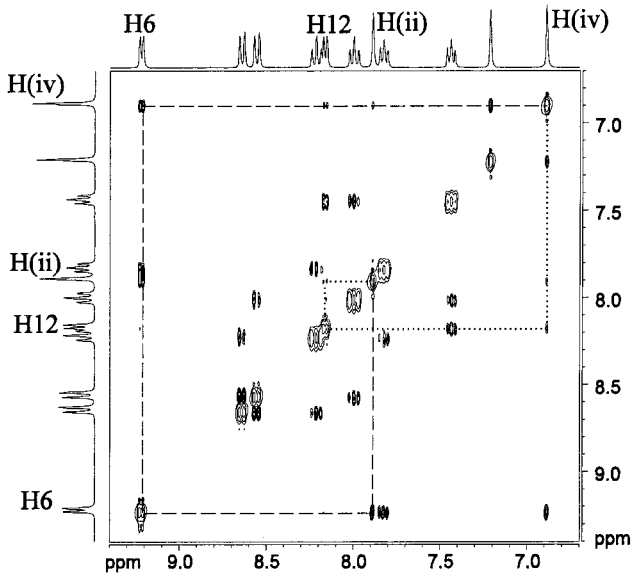


Figure 2. Aromatic region of the NOESY spectrum of *cis*-$[Ru(bpy)_2(MeIm)_2](PF_6)_2$, **1**, in acetone-$d_6$ at −75 °C, recorded with a mixing time of 1.0 s. The cross-peaks between the H6 and the H(ii) and H(iv) resonances, and between the H12 and the H(ii) and H(iv) signals are indicated with dashed and dotted lines, respectively.

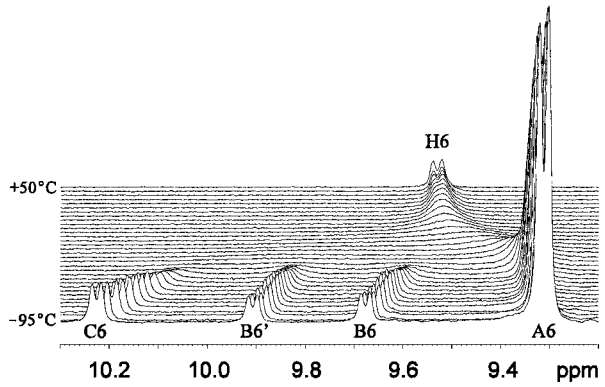


Figure 3. Variable-temperature ^{1}H NMR spectra of the H6 region of *cis*-$[Ru(bpy)_2(MeBim)_2](PF_6)_2$, **3**, in acetone-$d_6$ from −95 °C to +50 °C.

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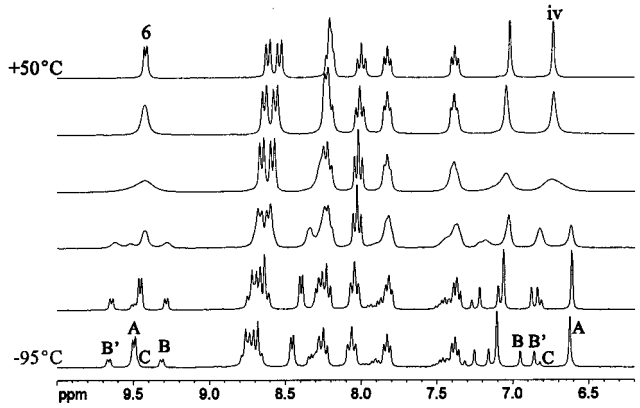


Figure 4. Variable-temperature ^{1}H NMR spectra of the aromatic region of *cis*-[Ru(bpy)$_2$(Me$_2$Im)$_2$](PF$_6$)$_2$, **2**, in acetone-d_6 from −95 °C to +50 °C.

Table 1. Selected Proton Resonances of the Atropisomers of Complex **3** and of Complex **4** at −95 °C and the Presence or Absence of Shielding Effects (sh), Deshielding Effects (desh), or No Effect (no) of the Imidazole Ligands (L-*mer* and L-*fac*) on the H6 and H6′ Signals

	3A	**3B**	**3B′**	**3C**	**4**
H(ii)/H(ii′)	8.86	8.87	8.68	8.91	3.76 (CH$_2$)
H(iv)/H(iv′)	7.59	7.56	7.15	7.18	6.55
H12/H12′	8.83	8.53	8.26	8.28	8.46
H6/H6′	9.30	9.62	9.90	10.23	9.23
L-*mer*	sh	no	sh	no	sh
L-*fac*	no	no	desh	desh	no

Complex **2** (Chart 5) has two untethered Me$_2$Im ligands and exhibits a ^{1}H NMR VT behavior (Figure 4) similar to that of **3** in the sense that, at low temperature, three different atropisomers can be identified, i.e., two HT isomers (C_2-symmetric, so there are 10 peaks for each in the aromatic region) and one HH isomer (20 peaks). The H6 resonances of the most abundant rotamer, **A**, and the least abundant rotamer, **C**, overlap at low temperatures, in contrast to the spectrum of complex **3**, where they are separated by almost 1 ppm. In the high-field area of the aromatic region, the Me$_2$Im signals of the H(iv) and H(v) protons of the different atropisomers are well separated at low temperatures and show a characteristic coalescing pattern on increasing temperature. Just as for the MeBim complex **3**, all the three possible atropisomers of **2** are found at low temperature, although their relative abundances are slightly different from those found for complex **3**: **A**, 55%; **B**, 40%; **C**, 5%.

Orientations of the R-imidazole Ligands. At low temperatures, complexes **2** and **3** show three sets of ^{1}H resonances belonging to three different atropisomers, **A**−**C**. For complex **3**, the orientations of the two MeBim ligands in the three rotamers have been determined[24] from typical NOE cross-peaks of the bpy H6 and H12 protons with the MeBim H(ii) and H(iv) protons. In particular, the cross-peaks of the H(iv) proton of the MeBim ligand of the most abundant atropisomer with the bpy H6 and H12 protons correspond to the HT conformation **A**, having both MeBim ligands oriented with their phenyl rings wedged between the two bpy ligands. Similar to the H(iv) proton in the main atropisomer, the H(ii) proton of the least abundant isomer, has cross-peaks with the bpy H6 and H12 protons, which corresponds to the **C** isomer, the HT isomer with the H(ii) sites of the two MeBim ligands wedged between the two bpy ligands. The nonsymmetric HH isomer (**B**) is readily recognized from the set with 20 aromatic peaks in which H6′ shows cross-peaks with both "tail" protons, H(iv) and H(iv′), and the H6 proton interacts with both "head" protons, H(ii) and H(ii′).

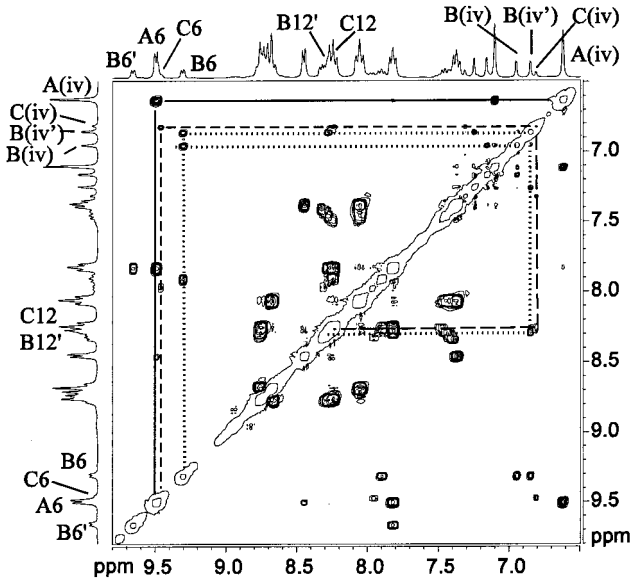


Figure 5. NOESY spectrum of *cis*-[Ru(bpy)$_2$(Me$_2$Im)$_2$](PF$_6$)$_2$, **2**, in acetone-d_6 at −95 °C, recorded with a mixing time of 1.0 s. Cross-peaks of the imidazole H(iv) with the H6 protons are indicated with a solid line (**2A**), a dashed line (**2C**), and a dotted line (**2B**) in the upper half of the spectrum; cross-peaks between the H(iv) and the H(12) of protons are indicated with a dashed (**2C**) and a dotted line (**2B**) in the lower half of the spectrum.

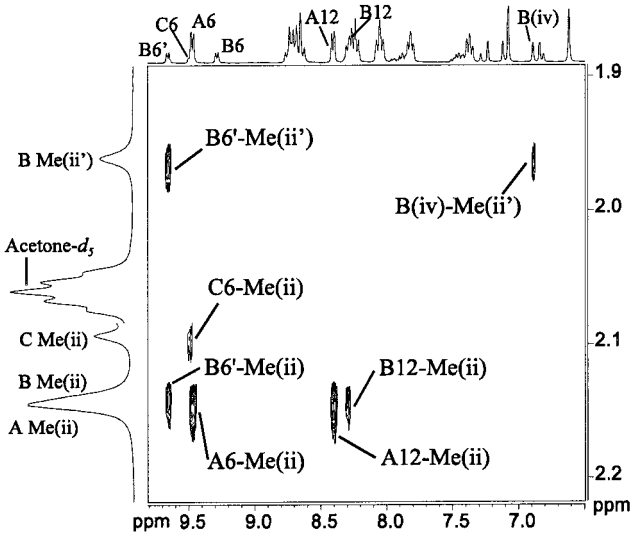


Figure 6. NOE level of the aliphatic region of the ROESY spectrum (mixing time 500 ms) of *cis*-[Ru(bpy)$_2$(Me$_2$Im)$_2$](PF$_6$)$_2$, **2**, in acetone-d_6 at −75 °C. (At −95 °C, the **B** Me(ii) and **A** Me(ii) signals overlap exactly, making interpretation of the cross-peaks difficult.)

In complex **2**, the Me(ii) part of each Me$_2$Im is defined as the "tail" as this is sterically the more demanding part of the ligand with respect to H(iv), which therefore has been defined as the "head" (Chart 2). One should be careful not to confuse the "head and tail" of each MeBim ligand in the above-discussed complex **3**, where H(iv) indicates the "tail" (phenyl ring). The NOESY spectrum of **2** at −95 °C is, in a sense, easier to interpret than that of **3** because there are less aromatic signals (Figure 5) than in the spectrum of the MeBim system; furthermore, in the aliphatic region, the Me(ii) singlets give very clear and informative cross-peaks (Figure 6). To determine the orientations of the Me$_2$Im ligands in the three atropisomers, the presence or absence of NOE cross-peaks for the signals of Me(ii) and H(iv) with the bpy H6 and H12 signals and the (other) Me$_2$-

Im Me(ii) and H(iv) signals was checked for each set of peaks. The most abundant atropisomer, **A**, shows interactions of Me(ii) with the H6 and H12 protons, while the H(iv) proton further interacts with the H6 resonance. From Chart 3, it can be readily seen that this is just what would be expected for atropisomer **A**. Similarly, the least abundant atropisomer can be attributed to the second HT isomer, **C**, having the Me(ii) peak coupling with the H6 peak, and the H(iv) peak further coupling with the H6 and H12 peaks. The set with 20 aromatic peaks is perhaps most illustrative, as all the proton signals are unique, due to the absence of the C_2-symmetry axis. For Me(ii), cross-peaks with H6′ and H12 are present, while H(iv) couples with H6, and Me(ii′); for the other Me_2Im ligand, Me(ii′) couples with H6′ and H(iv), whilst H(iv′) displays cross-peaks with H6 and H12′. All these NOE data unambiguously agree with the HH atropisomer **B**.

Marzilli et al. discuss[9,20] the differences in orientation between Me_2im and Me_3Bim (1,5,6-trimethylbenzimidazole) in *cis,cis,cis*-$[Ru(dmso)_2Cl_2(L)_2]$ complexes on basis of steric and electrostatic influences. In the *cis*-$[Ru(bpy)_2(L)_2]^{2+}$ system, no such electrostatic interactions are expected, as there are no coordinated chloride ions to which a partially positive NCHN of an imidazole ring can orient. Therefore, only steric interactions are expected to determine the possible formation of atropisomers and the ratio of the possible atropisomers in **2** and **3**. Interestingly, from a steric point of view, the Me(ii) side of Me_2Im appears very similar to the phenyl ring of MeBim; i.e., in the main conformer of **2**, the Me(ii) groups are pointing in the same directions as the phenyl ring of MeBim in its main conformer. This structural analogy is the same for the HH and the less abundant HT conformer. HH isomers of the cis bis adducts with untethered purine-like heterocycles are rare; it is therefore interesting to note that, in complexes of the type *cis*-$[Ru(bpy)_2(L)_2]^{2+}$, the HH rotamer is present in 40% abundance when L is Me_2Im (**2**) whereas this value is only 15% when L is MeBim (**3**).

Exchange Properties. Exchange spectroscopy is a very powerful tool for revealing the mechanism of atropisomerization due to ligand rotation. For the MeBim system **3**, it has been demonstrated that, at −95 °C, the three isomers cannot interconvert, whereas, at −75 °C, exchange cross-peaks are observed for the HH atropiosmer, **B**, with both HT atropisomers, **A** and **C**. Interestingly, no cross-peaks between the two HT isomers are found and also not between the HH peaks, indicating that only one MeBim ligand rotates at a time.[33] Apparently, **A** does not interconvert with **C** and **B** gives no exchange peaks with itself, i.e., the other (identical) HH isomer, indicating that atropisomerization must occur one step at a time, in which one benzimidazole flips around the Ru−N(iii) axis by approximately 180°. At −70 °C, the atropisomerization has already become so fast that exchange cross-peaks among all four H6 signals of **A**−**C** are found. For complex **2**, an exchange behavior similar to that of the MeBim complex **3** is found. At −95 °C, no exchange cross-peaks are found for the three atropisomers, whereas slightly higher temperature cross-peaks can be seen for the conformers. For complex **3**, the exchange mechanism can be best monitored via the H6 protons,[24] but for complex **2**, the H6 doublets of rotamers **A** and **C** overlap, which makes it difficult to assign the cross-peaks (Figure 7). However, it is apparent from this spectrum that the main HT atropisomer **A** interconverts with the HH atropisomer **B** and furthermore that **B** does not interconvert with itself at −75 °C. In the high-field area of the aromatic region, the imidazole H(iv) signals of all rotamers are also well separated from the other signals, and the EXSY spectrum of this region confirms that only interaction between the two main conformers, **A** and **B**, is occurring (Figure 7). Apparently there is no interaction between conformers **B** and **C**; this is different from the case of the MeBim complex, which shows interconversion of rotamer **B** with **A** as well as with **C**. This difference might well be due to the (relatively) low intensity of the signals of rotamer **C**.

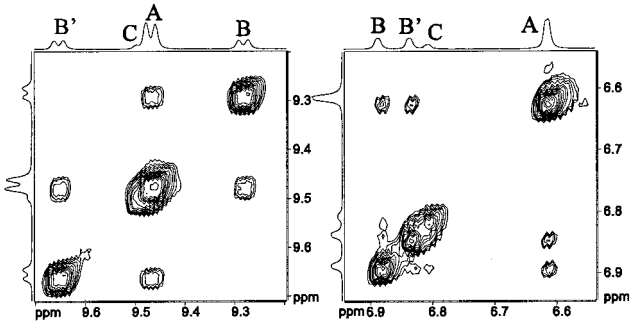


Figure 7. H6 region (left) and H(iv) region (right) of the ROESY spectrum (EXSY level) of *cis*-$[Ru(bpy)_2(Me_2Im)_2](PF_6)_2$, **2**, in acetone-$d_6$ at −75 °C, recorded with a mixing time of 500 ms.

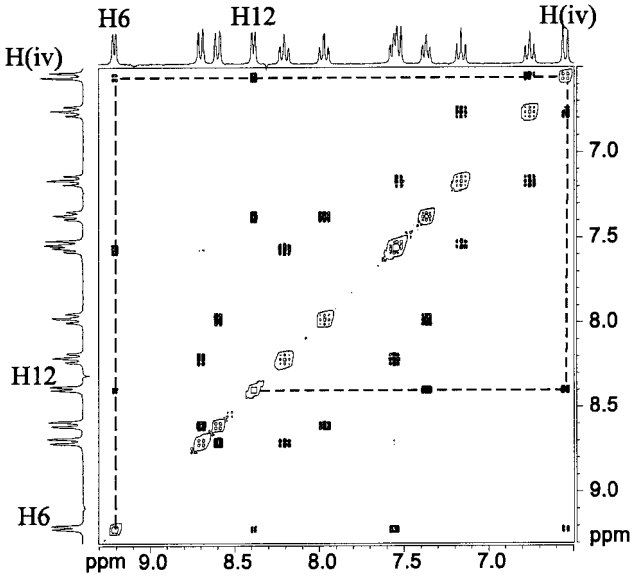
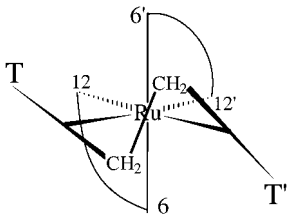


Figure 8. NOESY spectrum of *cis*-$[Ru(bpy)_2(mdbz)](PF_6)_2$, **4**, in acetone-$d_6$ at RT, recorded with a mixing time of 1.0 s. The NOE cross-peaks of H(iv) with the H6 and H12 protons are indicated with dashed lines.

Rigid, Nonrotating Ligands: *cis*-$[Ru(bpy)_2(mdbz)](PF_6)_2$. The aromatic region of the ^1H NMR spectrum of **4** shows only 12 signals for a total of 24 aromatic protons present (Figure 1). This indicates a 2-fold symmetry to be present in the compound, and therefore the two benzimidazole moieties have to be oriented in identical ways with respect to the C_2-symmetric $[Ru(bpy)_2]$. At higher and at lower temperatures, no changes occur in the spectra, indicating the absence of atropisomers. In the NOESY spectrum (Figure 8), the H(iv) protons clearly show strong cross-peaks with the H6 (of one bpy) and H12 of (the other) bpy, indicating the phenyl rings of the benzimidazoles to be wedged between the two bpy rings (Chart 6). In the aliphatic region, the protons of the bridging ethane moiety show a cross-peak with H6 (Supporting Information), similar to the H(ii) protons

(33) The HH conformer has no 2-fold symmetry axis, so there are no equivalent protons in this system. Therefore, if the HH isomer interconverted with itself, i.e., a double rotation of both MeBim's, exchange cross-peaks between **B** and **B**′ would be expected.

Chart 6. Schematic Representation of the Λ Enantiomer of *cis*-$[Ru(bpy)_2(mdbz)]^{2+}$



of MeBim in the **A** isomer of **3**. Thus, the orientation of the benzimidazole units can be concluded to be the same as that of the MeBim ligands in the most abundant HT atropisomer of **3** (with the benzimidazoles untethered). Another informative signal of **4** is that of H(iv), which at 6.55 ppm is shifted significantly upfield with respect to the H(iv) resonance of **3A**. This difference (1.0 ppm) is most likely due to the benzimidazole phenyl ring in the former being oriented slightly more above the (shielding) pyridine ring of one bpy instead of being wedged between the two bpy ligands as in the latter (compare Charts 6 and 3, respectively). From a space-filling model, this "**A**" orientation was also anticipated; an orientation of the benzimidazole moieties of mdbz on a *cis*-$[Ru(bpy)_2]^{2+}$ unit like that of the MeBim ligands in one of the two less abundant atropisomers of **3** would create too much stress on the ethane bridge. In fact, mdbz, as a dinucleating ligand, could also have both benzimidazole groups coordinating with a different $[Ru(bpy)_2]$ unit, giving rise to dinuclear or polynuclear complexes. This is unlikely for complex **4** as prepared in this study, with the $[Ru(bpy)_2]$ moiety being chiral; a mixture of (dia)stereoisomers would then be expected, a phenomenon that would have been immediately seen in the NMR spectra.[34]

bpy as a Spectator Ligand. (De)Shielding Effects on the H6 Protons. In ^{1}H NMR investigations of the fluxional behavior of guanine derivatives in platinum complexes, the main focus has been on only one proton, i.e., H8 of the purine 5 ring. Benzimidazole derivatives are very useful purine analogues for such ^{1}H NMR investigations because, besides the imidazole proton (H(ii)), they have an additional proton on the six-membered ring, H(iv), that can act as a probe proton.[9,20] Alternatively, it now appears most informative to determine whether the rotating ligands characteristically influence the resonances of some protons in the nonrotating backbone system.

A very interesting feature in the $[Ru(bpy)_2(RIm)_2]^{2+}$ systems is the orientation of the imidazole ligands, which characteristically influence the resonance signals of the bpy H6 protons. For complexes **1**−**4**, the bpy H6 signals are found at low field, well separated from the other signals (Figure 1). For the three atropisomers of compound **3**, the H6 resonances are significantly influenced by the (presence or absence of the) shielding effect of the phenyl ring of one of the benzimidazoles and by the deshielding effect of the other benzimidazole (Table 1). Both MeBim ligands in **3** can have two types of interactions with one H6 proton, and interestingly, in the three atropisomers, all four possible combinations are present. In conformer **A**, the H6 protons (9.30 ppm) are shielded by the benzimidazoles which are in a *mer* position with respect to the bpy ligands and are not influenced by the six-membered ring of the other benzimidazole. In conformer **B**, the B6 proton (9.62 ppm) is not influenced by either of the two benzimidazole six-membered rings, while the B6′ proton (9.90 ppm) is shielded by the *mer*-positioned benzimidazole (B(iv−vii)) but deshielded by the *fac*-oriented benzimidazole (B(iv′−vii′)). In conformer **C**, finally, the H6 protons (10.23 ppm) are not influenced by the six-membered ring of the *mer*-coordinated benzimidazole but are deshielded by the six-membered ring of the *fac*-coordinated benzimidazole. Therefore, it can be concluded that, in **3**, the deshielding of the phenyl ring of a *fac*-coordinated benzimidazole has a larger influence on the H6 signal than the shielding effect of the phenyl ring of a *mer*-coordinated benzimidazole. Because the benzimidazole moieties in **4** are oriented as in isomer **3A**, the H6 protons of **4** are expected to be influenced by the shielding effects of the phenyl rings of the benzimidazoles in a manner similar to that just described for this HT isomer of **3**. This appears to correlate well, as the H6 signal of isomer **3A** is found at 9.3 ppm and the H6 signal of **4** is found at 9.2 ppm. So, in a sense, bpy can be regarded as a spectator ligand, a nonrotating ligand that can provide information on the orientation of a (fluxional) bicyclic ligand via the H6 "probe" proton.

Conclusions

Studies of the coordination of heterocyclic nitrogen ligands to *cis*-$[Ru(bpy)_2Cl_2]$ using various approaches[31,35,36] have led to increased knowledge of the spectroscopic, (photo)physical, and (photo)chemical properties of complexes of the type *cis*-$[Ru(bpy)_2(RIm)_2]^{2+}$. As far as we are aware, none of the prior studies focused on the fluxional behavior of the monodentate ligands in complexes of this type. Our interest in *cis*-dichlororuthenium(II) complexes of the type *cis*-$[Ru(BL)_2Cl_2]$, with BL being a heterocyclic bidentate ligand, such as bpy, phenantroline, or 2-(phenylazo)pyridine (azpy), stems from the interesting coordination properties of these complexes with regard to DNA[37−40] and DNA model bases[41,42] and from the remarkably high cytotoxicity of only one of these *cis*-dichloro complexes, namely, α-$[Ru(azpy)_2Cl_2]$.[43]

In the present study, the coordination properties and rotational behaviors of three different heterocyclic monodentate nitrogen ligands in the *cis*-$[Ru(bpy)_2(L)_2](PF_6)_2$ system are described. From the ^{1}H NMR spectra of these bifunctionally coordinated complexes, it can indeed be concluded that, sterically, *cis*-$[Ru(bpy)_2(Cl_2)]$ is a borderline case with respect to the binding to two heterocyclic bases; this is reflected in the very different fluxional behaviors of the monodentate ligands. For the complex *cis*-$[Ru(bpy)_2(MeIm)_2](PF_6)_2$, the ^{1}H NMR experiments conducted at various temperatures indicate that the 1-methylimidazoles are coordinated via their N(iii) atoms and that they can both freely rotate on the NMR time scale around their Ru−N axes, at high as well as at low temperatures. Two other sterically more demanding bases (Me_2Im and MeBim) can be oriented only in two restricted ways on the ruthenium. In solution, all three possible atropisomers are present, i.e., two symmetric HT

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rotamers and one asymmetric HH rotamer. At 55 °C, the atropisomers are in fast exchange according to the NMR spectra, while, at −95 °C, the three different atropisomers cannot exchange among themselves and the mutual orientation of all the ligands was determined using NOESY data.

In conclusion, complexes of the type *cis*-$[Ru(BL)_2Cl_2]$ are suitable compounds for investigating in detail the fluxional behaviors of N-heterocycles in octahedral complexes. Variation of the bidentate ligands in *cis*-$[Ru(BL)_2(L)_2]^{2+}$ complexes, the use of mixed bidentate ligands, *cis*-$[Ru(BL)(BL')(L)_2]^{2+}$, introducing mixed monodentate ligands *cis*-$[Ru(BL)_2(L)(L')]^{2+}$, and of course the combination of these two, *cis*-$[Ru(BL)(BL')(L)(L')]^{2+}$, will provide a large field of complexes in which the factors influencing the coordination properties and the orientational and fluxional behaviors of heterocyclic (lopsided) monodentate ligands can be thoroughly studied. Furthermore, the introduction of C_2-symmetric monodentate ligands and of chiral ligands will make this system even more versatile. Studies of these types of complexes are currently being pursued.

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Supporting Information Available: NOESY spectra of **2** and **3** at 50 °C and of **4** at RT and a table of ^{1}H NMR data for **1** and **4** at RT and for **2** and **3** at 50 °C. This material is available free of charge via the Internet at http://pubs.acs.org.

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