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# Isomerization Dynamics in Homo- and Heterochiral Atropoisomer Copper(I) Diimine Complexes: A 2D EXSY NMR Study

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Two-dimensional exchange NMR spectroscopy has been employed to study the isomerization process of copper(I) complexes formed upon complexation of $Cu^+$ with a racemic mixture of the atropoisomer diimine benzimidazole–pyridine ligands **1**–**3** and evaluate the configurational stability of the pseudotetrahedral complexes $[Cu(\mathbf{1}–\mathbf{3})_2]PF_6$. Racemization of the heterochiral isomers *RS*Λ/*RS*Δ proceeds through an intramolecular ligand rearrangement on a time scale of about 1.9 $s^{-1}$ for **1**, 4.4 $s^{-1}$ for **2**, and 0.3 $s^{-1}$ for **3** in $CD_2Cl_2$ at room temperature. The intramolecular Λ/Δ isomerizations in the homochiral diastereoisomers *RR*Δ/*SS*Λ and *RR*Λ/SSΔ of $[Cu(\mathbf{1})_2]PF_6$ proceed at room temperature on a time scale of about 0.6 $s^{-1}$ for the conversion of *RR*Δ/*SS*Λ into *RR*Λ/SSΔ and 13 $s^{-1}$ for the conversion of *RR*Λ/SSΔ into *RR*Δ/*SS*Λ. The kinetics of these intramolecular exchange processes were found to be sensitive to the stabilizing interligand $\pi$-stacking interactions that develop within the $[Cu(\mathbf{1}–\mathbf{3})_2]^+$ structure and to the bulkiness of the benzimidazole aryl substituents. The kinetics of racemization in the heterochiral *RS*Λ/*RS*Δ isomers of $[Cu(\mathbf{3})_2]PF_6$ with the bulky cumyl-derived ligand were 1 order of magnitude lower than in $[Cu(\mathbf{2})_2]PF_6$ with the tolyl-based ligand. Slower intermolecular ligand exchanges between all the isomers have also been shown to occur at ambient temperature in $CD_2Cl_2$ through complete ligand dissociation. Free energies at 298 K varying between 66.7 and 74.4 kJ·mol$^{-1}$ and entropies varying between –26.4 and 28.3 J·K$^{-1}$·mol$^{-1}$ were determined for the intramolecular Λ/Δ isomerizations. For the intermolecular ligand exchanges free energies at 298 K varying between 55.6 and 62.5 kJ·mol$^{-1}$ and entropies varying between –97.9 and –74.5 J·K$^{-1}$·mol$^{-1}$ were measured.

## Introduction

Copper(I) complexes $[CuL_2]^+$ of diimine ligands (L) are an important class of coordination compounds not only because they have interesting photophysical and redox properties[1] but also because they have found important applications in asymmetric catalysis[2] and in the preparation of supramolecular assemblies.[3] The pseudotetrahedral $[CuL_2]^+$ complexes usually exhibit low configurational stability in solution. Isomerization at the copper center may be slowed by introducing bulky substituents in positions adjacent to the N-coordinating atoms to provide steric inhibition of the geometric reorganization that occurs upon isomerization.[4,5]

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Other factors such as the flexibility of the diimine (2,2′-bipyridines offer the possibility of rotation around the 2,2′-bond compared to the rigid 1,10-phenanthroline) have been shown to favor the isomerization,[6] while on the contrary interligand $\pi$-stacking interactions will stabilize the $[CuL_2]^+$ structure.[1g,7] A detailed study of isomerization processes in silver(I) and copper(I) complexes $[ML_2]^+$ was reported in 1984 by Van Koten and co-workers.[5] *o,o*′-Substituted-pyridine imine ligands bearing enantiotopic or chiral substituents were used to induce NMR differentiation in the $[ML_2]^+$ spectra. Because of the lack of coupling information with the $Cu^+$ ion in the spectra of the $[CuL_2]^+$ complexes and because these complexes were configurationally stable in solution (up to 310 and 330 K in $CD_2Cl_2$ and MeOD, respectively), isomerizations were not observed by VT-NMR. However, the study of the less stable analogous $[AgL_2]^+$ complexes by VT-NMR have shown that racemization occurs mainly by a fast intramolecular ligand exchange proceeding, most probably through the breaking of one pyridine−silver bond. Interestingly, because of coupling information of some ligand proton resonances with the silver(I) ion ($I = 1/2$), slower intermolecular ligand exchanges implying complete ligand dissociation were also evidenced. No values of activation parameters were reported for these exchanges. VT-NMR was also used by Thummel and co-workers to study the kinetics of racemization in $[CuL_2]^+$ complexes with phenanthroline ligands bearing enantiotopic methyl groups and 2,2′-bipyrimidines with substituents at the 4,4′ and 6,6′ positions that become inequivalent when two ligands are bound to a single metal in a tetrahedral fashion.[4] The isomerization rates were found to be fast at ambient temperature allowing the determination of the racemization barriers by VT-NMR. Free energies ($\Delta G^{\ddagger}$) around 61.4−63.5 kJ·mol$^{-1}$ were measured in $CDCl_3$ for 1,10-phenanthroline and 2,2′-bipyrimidine derivatives. The lower values measured in $CD_3CN$ solutions (around 56.5−58.5 kJ·mol$^{-1}$) were attributed to solvent participation in the exchange process. Recently, an original approach was reported by Sauvage, Lacour, and co-workers using the chiral TRISPHAT counteranion as the source of NMR differentiation, thus allowing the determination of the racemization barriers of ligands deprived of enantiotopic or chiral substituents.[8] Enantiopure Δ-TRISPHAT was used as an effective chiral shift reagent for a series of $[CuL_2]^+$ of unsymmetrical 1,10-phenanthrolines, 2,2′-bipyridines, and 2-iminopyridines ($\Delta G^{\ddagger} \sim 58.2-71.8$ kJ·mol$^{-1}$). Chiral diimine ligands have therefore, to the best of our knowledge, never been used to study the exchange processes in pseudotetrahedral $[CuL_2]^+$ complexes. One should bear in mind that if enantiopure chiral ligand are employed and if high diastereoselective complexation occurs, only the signals of the major diastereoisomer will be observed, making this approach nonapplicable. Therefore, the use of chiral ligands will be valuable for such studies only if modest diastereoselective complexations occur. In that case using a racemic mixture of chiral ligands will generate a slightly more complicated system than using an enantiopure ligand, as three couples of enantiomers (*RR*Δ/*SS*Λ, *RR*Λ/*SS*Δ, and *RS*Λ/*RS*Δ) with theoretically distinct NMR signals could be formed. On the other hand, if the exchange rates lie in the NMR time scale range, this should permit not only the study of the Λ/Δ isomerizations in both homo- and heterochiral complexes but also the study of intermolecular ligand exchanges. We previously reported that upon complexation of $Cu^+$ with 2 equiv of the racemic atropoisomer diimine ligand **1** (Figure 1), the three enantiomeric couples *RR*Δ/*SS*Λ, *RR*Λ/*SS*Δ, and *RS*Λ/*RS*Δ (Figure 2) were formed in ratios of 49, 4, and 47% respectively.[9] Using the bulky cumyl-based ligand **3** the formation of the homochiral *RR*Δ/*SS*Λ isomers was highly favored (95%). Due to important steric interligand interactions, the heterochiral isomers *RS*Λ/*RS*Δ represented 5% of the mixture while the homochiral *RR*Λ/*SS*Δ were not detected. We report herein a detailed two-dimensional exchange $^1$H NMR spectroscopy (2D EXSY) study of the isomerization processes for copper complexes $[Cu(\mathbf{1}-\mathbf{3})_2]^+$. The exchange kinetics and activation parameters of the isomerizations in both homochiral and heterochiral complexes have been evaluated for the first time with $[CuL_2]^+$ complexes. The occurrence of both intramolecular Λ/Δ isomerizations and intermolecular ligand exchanges at ambient temperature in $CD_2Cl_2$ were revealed. The importance of the interligand

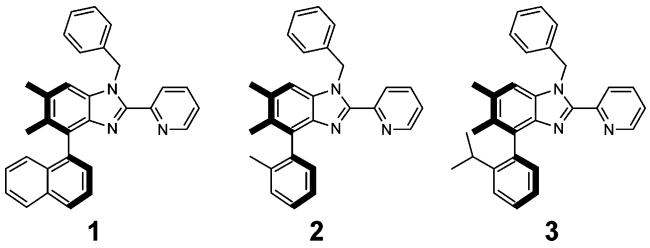


**Figure 1.** Molecular structure of the atropoisomer diimine ligands **1**−**3** (*R* isomers).

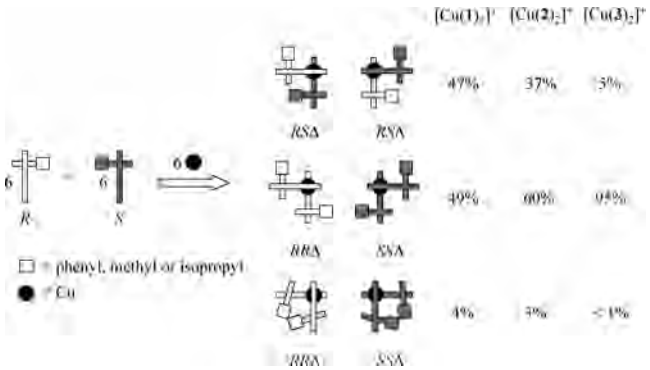


**Figure 2.** Possible isomers formed upon complexation of the diimines **1**−**3** with $Cu^+$ and isomeric ratios measured by $^1$H NMR in $CD_2Cl_2$ for the complexes $[Cu(\mathbf{1}-\mathbf{3})_2]PF_6$.

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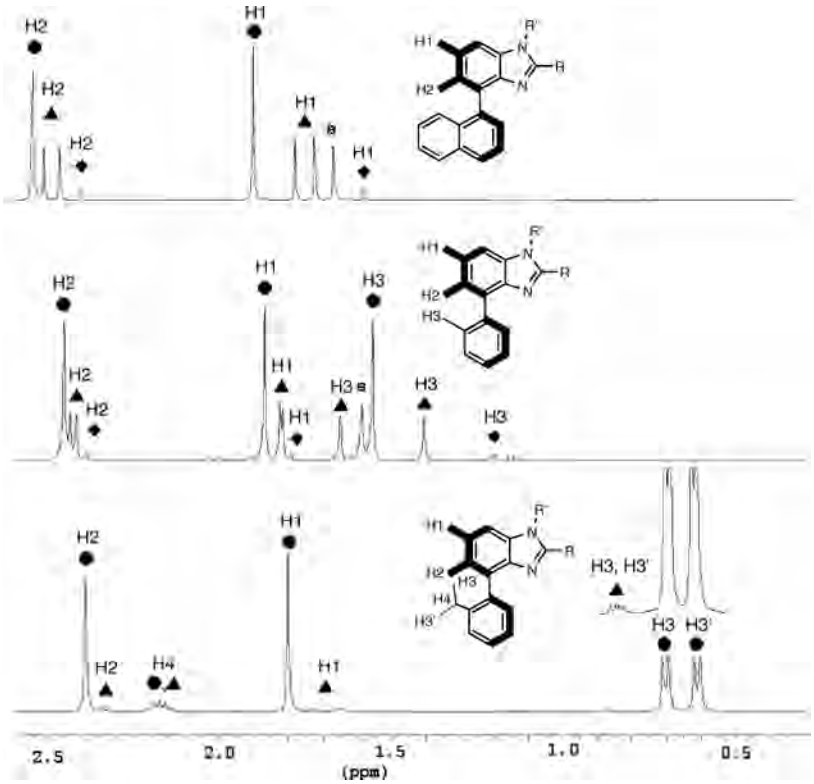


**Figure 3.** $^1$H NMR spectra at 400 MHz in $CD_2Cl_2$ of the methyl protons of [Cu(**1**)$_2$]$PF_6$ (233 K, top), [Cu(**2**)$_2$]$PF_6$ (253 K, middle), and [Cu(**3**)$_2$]$PF_6$ (233 K, bottom): ●, $CH_3$ resonances for *RR*Δ/*SS*Λ; ♦, for *RR*Λ/*SS*Δ; ▲, for *RS*Λ/*RS*Δ (s = residual water).

$\pi$-stacking and steric interactions in such processes has been highlighted.

## Results and Discussion

**Background.** The complete proton assignments in $CD_2Cl_2$ for the complexes [Cu(**1**−**3**)$_2$]$PF_6$ have been previously described.[9] The isomeric ratios for the three couples of enantiomers were conveniently measured by $^1$H NMR spectroscopy as high anisotropy was observed in the $^1$H NMR spectra of [Cu(**1**−**3**)$_2$]$PF_6$. This anisotropy is particularly striking for the proton resonances of the methyl groups that lie in very different chemical environments for each couple of enantiomers due to strong interligand interactions (Figure 3). Thus, the low-temperature $^1$H NMR spectrum of the methyl region of [Cu(**1**)$_2$]$PF_6$ displays eight well-resolved peaks, as expected for a mixture of the isomers *RR*Δ/*SS*Λ ($C_2$ symmetry, two methyl resonances), *RR*Λ/*SS*Δ ($C_2$ symmetry, two methyl resonances), and *RS*Λ/*RS*Δ ($C_1$ symmetry, four methyl resonances). As evidenced in its $^1$H NMR spectrum, [Cu(**3**)$_2$]$PF_6$ with the most crowded cumyl-derived ligand was mainly present in $CD_2Cl_2$ solution as the homochiral racemate *RR*Δ/*SS*Λ with a measured diastereoisomeric excess of 95% (Figure 3). The heterochiral isomers *RS*Λ/*RS*Δ represented 5% of the mixture, while the *RR*Λ/*SS*Δ isomers were not detected. Owing to lower interligand steric repulsions within their structure, the homorecognition for [Cu(**1**)$_2$]$PF_6$ and [Cu(**2**)$_2$]$PF_6$ was less pronounced as diastereoisomeric excesses of 6 and 26% were measured, respectively. For this study the methyl resonances were chosen as $^1$H NMR spies to record the 2D EXSY NMR spectra.

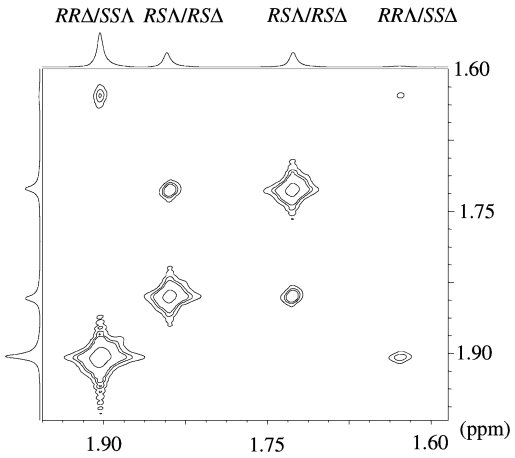


**Figure 4.** H1 methyl region of the EXSY $^1$H NMR spectrum of [Cu(**1**)$_2$]$PF_6$ in $CD_2Cl_2$ at 298 K and a mixing time of $\tau_m$ = 75 ms.

**Complexes' Isomerization Pathways.** A representative example of a two-dimensional exchange spectrum of the H1 methyl region of [Cu(**1**)$_2$]$PF_6$ in $CD_2Cl_2$ solution at a temperature of 298 K and a mixing time of $\tau_m$ = 75 ms is shown in Figure 4. Using this relatively short mixing time, the spectrum exhibits off-diagonal peaks between both the H1 and H2 protons (not shown for H2) of the *RR*Λ/*SS*Δ and *RR*Δ/*SS*Λ diastereoisomers. Due to their $C_1$ symmetry, the heterochiral enantiomers *RS*Λ and *RS*Δ have four inequivalent methyl groups that theoretically should allow the direct visualization of the *RS*Λ ⇆ *RS*Δ racemization and determination of the kinetics of this process. Accordingly, exchange cross-peaks between the two differentiated H1 protons (also seen with the two H2 resonances, not shown)

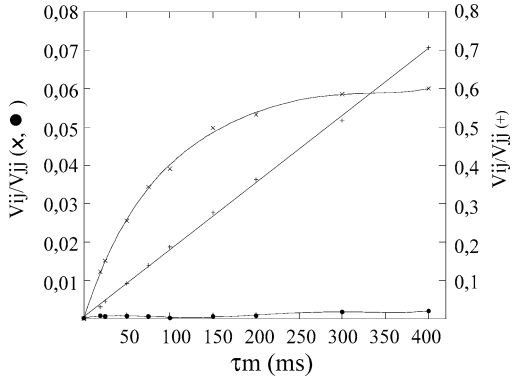


**Figure 5.** Buildup curves for $[Cu(\mathbf{1})_2]PF_6$ displaying the area ratio of the cross-peak volumes $V_{ij}$ normalized to the auto-peak $V_{jj}$ against the mixing time $\tau_m$: +, *RS*Λ ⇆ *RS*Δ; ×, *RR*Δ/*SS*Λ → *RR*Λ/*SS*Δ; ●, *RR*Δ/*SS*Λ → *RS*Λ/*RS*Δ.

of the heterochiral *RS*Λ and *RS* enantiomers are obtained. Thus, Λ/Δ isomerizations occur in $CD_2Cl_2$ at ambient temperature in both homo- and heterochiral isomers of $[Cu(\mathbf{1})_2]PF_6$.

The profile analysis of the buildup curves displayed in Figure 5, which provide the cross-peak volumes $V_{ij}(t_m)$ normalized to the auto-peak $V_{jj}(t_m)$ as a function of the mixing time $\tau_m$, allows a direct assessment as to whether the isomerizations occur through an intramolecular ligand rearrangement (direct ligand exchange) or through an intermolecular process, implying complete ligand dissociation.[10]

The *RR*Δ/*SS*Λ → *RR*Λ/*SS*Δ and *RS*Λ ⇆ *RS*Δ conversions for $[Cu(\mathbf{1})_2]PF_6$ clearly display nonzero slopes at low mixing time values revealing direct interconversions through intramolecular ligand exchanges. At $\tau_m = 75$ ms, correlation peaks between the H1 protons of the homochiral and heterochiral isomers were not observed (Figure 4). However, after an induction period of approximately 200 ms correlation peaks of low intensities were observed traducing a multistep relayed magnetization transfer between the isomers *RR*Δ/*SS*Λ and *RS*Λ/*RS*Δ. Thus, a multistep exchange pathway between homo- and heterochiral species implying complete ligand dissociation is observed, the occurrence of a bimolecular process involving a dicopper intermediate complex being excluded since buildup curves with nonzero slopes (revealing direct exchanges) should be observed with such a mechanism. On the other hand the Δ/Λ isomerization in both the homochiral and heterochiral complexes proceeds through intramolecular rearrangement. Analysis of the profiles of the buildup curves with ligands **2** and **3** (obtained from the 2D EXSY of the H3 methyl region) revealed the same behavior,[11] leading to the isomer exchange pathway proposal presented in Figure 6.

**Kinetics of the Intramolecular Δ/Λ Isomerizations.** The cross-peak and auto-peak areas obtained at various mixing time delays gave rise to 4 × 4 matrixes for $[Cu(\mathbf{1})_2]PF_6$ and 3 × 3 matrixes for $[Cu(\mathbf{2})_2]PF_6$ and $[Cu(\mathbf{3})_2]PF_6$. These

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(11) The $^1H$ NMR spectra of $[Cu(\mathbf{1}-\mathbf{3})_2]PF_6$ recorded in $CD_2Cl_2$ at 298 K and the buildup curves for $[Cu(\mathbf{2})_2]PF_6$ and $[Cu(\mathbf{3})_2]PF_6$ are given in the Supporting Information.

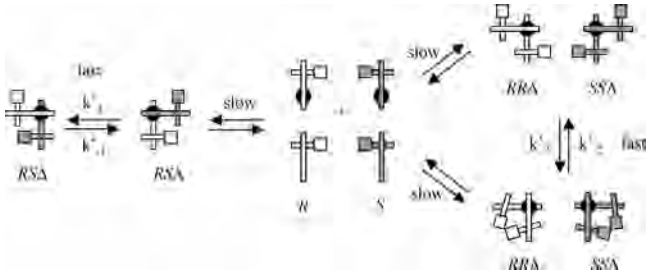


**Figure 6.** Isomer exchange pathways for $[Cu(\mathbf{1}-\mathbf{3})_2]PF_6$ in $CD_2Cl_2$.

**Table 1.** Rate Constants at 298 K for the Intramolecular Δ/Λ Isomerizations Determined by Least-squares Fitting of the Experimental H1 and H2 Peak Intensities

| Complex | $k'_1/s^{-1}$ | $k'_{-1}/s^{-1}$ | $k'_2/s^{-1}$ | $k'_{-2}/s^{-1}$ |
|---|---|---|---|---|
| $[Cu(\mathbf{3})_2]^+$ | $0.33 \pm 0.08$ | NA[a] | | |
| $[Cu(\mathbf{2})_2]^+$ | $4.36 \pm 1.00$ | $4.4 \pm 1.00$ | NA[b] | NA[b] |
| $[Cu(\mathbf{1})_2]^+$ | $1.93 \pm 0.03$ | $1.91 \pm 0.04$ | $0.57 \pm 0.13$ | $12.7 \pm 0.41$ |

[a] Not available because of overlapping *RR*Δ and *RS*Λ/*RS*Δ H3 resonances.[11] [b] Not available at 298 K because of overlapping *RR*Λ/*SS*Δ and *RR*Δ/*SS*Λ resonances.[11]

matrixes were used to determine the rate constant values reported in Table 1 using the method developed by Perrin and Gipe.[12] The relatively large standard error measured for the rate constant $k'_2$ for $[Cu(\mathbf{1})_2]PF_6$ was due to the low concentration of the *RR*Δ/*SS*Λ enantiomers (4% of the mixture).

One can compare the rates of the Λ/Δ isomerizations in the heterochiral *RS* isomers of complexes $[Cu(\mathbf{3})_2]PF_6$ and $[Cu(\mathbf{2})_2]PF_6$. The racemization occurs approximately 10 times faster for $[Cu(\mathbf{2})_2]PF_6$ showing clearly that the rate of this intramolecular isomerization process is very sensitive to the bulkiness of the phenyl ring *ortho*-substituents, the isopropyl group being much bulkier than the methyl group. An intramolecular isomerization would require a drastic rearrangement of the coordination sphere, particularly with these ligands in which a chirality axis is perpendicular and close to the complexation site axis, thus preventing the intermediacy of a square-planar geometry during the isomerization process. As no complete ligand loss was observed, we assume that isomerization will require the decoordination of one ligand−metal bond followed by a concerted rearrangement of the coordination sphere favored by the possible rotation around the pyridine−benzimidazole bond.

If only the phenyl *ortho*-substituent effect on the intramolecular racemization rates is considered, one might expect to observe a lower rate constant for $[Cu(\mathbf{2})_2]PF_6$, which has the bulkier methyl *ortho*-substituent compared to $[Cu(\mathbf{1})_2]PF_6$. The slightly higher bulkiness of the tolyl group with respect to the naphthyl resulted in the higher diastereoisomeric excess measured for $[Cu(\mathbf{2})_2]PF_6$ compared to $[Cu(\mathbf{1})_2]PF_6$ (26 and 6%, respectively). Nonetheless, the racemization rate of the heterochiral *RS* isomers of $[Cu(\mathbf{2})_2]PF_6$ was found to be two times faster than for $[Cu(\mathbf{1})_2]PF_6$. This strongly suggests that the interligand $\pi$-stacking interactions that specifically develop within the complex structure of [Cu-

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**Table 2.** Rate Constants at 298 and 263 K for the Ligand Exchanges and Λ/Δ Isomerizations in $CD_2Cl_2$ Solution of $[Cu(\mathbf{1})_2]PF_6$ in the Presence of Excess Ligand **1** (40 mol %) Determined by the Resolution the Exchange Matrices Obtained at Different Mixing Times

| k | 298 K[a] | 263 K[a] |
|---|---|---|
| $k_1$ | $75 \pm 8$ $M^{-1}\cdot s^{-1}$ | $7.7 \pm 1.6$ $M^{-1}\cdot s^{-1}$ |
| $k_{-1}$ | $68 \pm 12$ $M^{-1}\cdot s^{-1}$ | $7.0 \pm 2.1$ $M^{-1}\cdot s^{-1}$ |
| $k_2$ | $148 \pm 15$ $M^{-1}\cdot s^{-1}$ | $19.8 \pm 2.0$ $M^{-1}\cdot s^{-1}$ |
| $k_{-2}$ | $138 \pm 14$ $M^{-1}\cdot s^{-1}$ | $21.2 \pm 2.1$ $M^{-1}\cdot s^{-1}$ |
| $k_3$ | $906 \pm 130$ $M^{-1}\cdot s^{-1}$ | $188 \pm 24$ $M^{-1}\cdot s^{-1}$ |
| $k_{-3}$ | $1109 \pm 120$ $M^{-1}\cdot s^{-1}$ | $169 \pm 23$ $M^{-1}\cdot s^{-1}$ |
| $k'_1/s^{-1}$ | $1.86 \pm 0.05$ $s^{-1}$ | $0.054 \pm 0.008$ $s^{-1}$ |
| $k'_{-1}/s^{-1}$ | $1.84 \pm 0.05$ $s^{-1}$ | $0.053 \pm 0.008$ $s^{-1}$ |
| $k'_2/s^{-1}$ | $0.57 \pm 0.13$ $s^{-1}$ | $0.012 \pm 0.003$ $s^{-1}$ |
| $k'_{-2}/s^{-1}$ | $12.8 \pm 0.9$ $s^{-1}$ | $0.2 \pm 0.03$ $s^{-1}$ |

[a] Sample preparation: $[Cu(\mathbf{1})_2]PF_6$ (11.03 μmol, 10.4 mg) + **1** (4.25 μmol, 1.87 mg) in $CD_2Cl_2$ (450 μL).

$(\mathbf{1})_2]PF_6$ because of the presence of the polycyclic aromatic hydrocarbon naphthyl substituents will stabilize the $[Cu(L)_2]^+$ structure thus disfavoring the isomerization process. As previously shown in the crystal structure of the homochiral isomer Δ-$[Cu(^R\mathbf{1})_2]PF_6$, each naphthyl group π-stacks with the pyridyl group of the other ligand with plane to plane distances of around 3.5 Å.[9] In the heterochiral complexes, one naphthyl will stack with a pyridine while the other naphthyl will stack with the benzimidazole moiety. Much less favorable π−π stacking interactions are expected with the tolyl-based ligand as the methyl group is present in place of the phenyl ring which is largely responsible for the π-stacking interactions in $[Cu(\mathbf{1})_2]PF_6$. In $[Cu(\mathbf{3})_2]PF_6$ the exchange barrier associated with the steric hindrance due to the very bulky cumyl group is expected to be much higher than the stabilization energy associated with the π-stacking interactions found in $[Cu(\mathbf{1})_2]PF_6$. This explains why the rate of racemization for $[Cu(\mathbf{3})_2]PF_6$ is much smaller than the rate constant found for $[Cu(\mathbf{1})_2]PF_6$, even in the absence of π-stacking interactions

The conversion of the *RR*Δ/*SS*Λ isomers into their *RR*Λ/*SS*Δ diastereoisomers in $[Cu(\mathbf{1})_2]PF_6$ was found to be approximatively 20 times slower than the reverse reaction ($k'_2$ compared to $k'_2$). The homochiral *RR*Λ/*SS*Δ isomers that represent only 4% of the mixture compared to 49% for *RR*Δ/*SS*Λ are destabilized by strong interligand steric interactions between the naphthyl groups, thus favoring the intramolecular isomerization process into the more stable *RR*Δ/*SS*Λ isomers.

**Kinetics of the Intermolecular Ligand Exchanges.** As evidenced from the dynamic NMR studies performed on $[Cu(\mathbf{1})_2]PF_6$, slow conversions between homo- and heterochiral species occur in $CD_2Cl_2$ at ambient temperature through the intermediacy of the free ligand. To determine the kinetics of the intermolecular ligand exchange process, dynamic $^1H$ NMR at different mixing times has been performed on $[Cu(\mathbf{1})_2]PF_6$ by adding free ligand **1** (40 mol %) to a $CD_2Cl_2$ solution of the complex (Table 2). As shown on the EXSY NMR spectrum recorded with $\tau_m = 75$ ms, off-diagonal peaks between the H1 protons of the homochiral diastereoisomers and between the H1 protons of the heterochiral enantiomers are still observed (Figure 7). Additionally, off-diagonal peaks are now observed between the free ligand

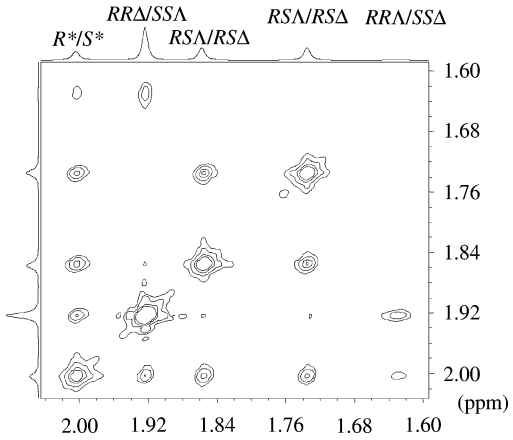



**Figure 7.** H1 methyl region of $[Cu(\mathbf{1})_2]PF_6$ EXSY NMR spectrum recorded at 298 K in $CD_2Cl_2$ with 75 ms mixing time in the presence of an excess of **1** (*R**/*S**, 40 mol %).

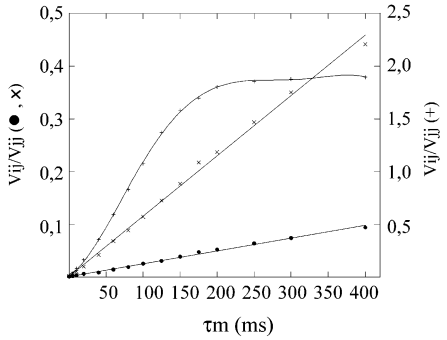



**Figure 8.** Buildup curves displaying the area ratio of the cross-peak volumes $V_{ij}$ normalized to the auto-peak $V_{jj}$ against the mixing time $\tau_m$ for the exchange between the free ligand *R**/*S** and the different isomers of $[Cu(\mathbf{1})_2]PF_6$: ●, exchange with *RS*Λ/*RS*Δ; +, exchange with *RR*Δ/*SS*Λ; ×, exchange with *RR*Λ/*SS*Δ.

H1 protons and the H1 protons of all the $[Cu(\mathbf{1})_2]PF_6$ isomers present in solution.

The buildup analysis of cross-peak versus auto peak areas observed between the free ligand *R**/*S** and all the isomers are presented in Figure 8. Resolution of the (5 × 5) matrixes obtained at different mixing times gave access to the observed rate constants $k_{obs_1} = k_1[RR\Delta/SS\Lambda]$, $k_{obs_{-1}} = k_{-1}[R/S]$, $k_{obs_2} = k_2[RS\Lambda/RS\Delta]$, $k_{obs_{-2}} = k_{-2}[R/S]$, $k_{obs_3} = k_3[RR\Lambda/SS\Delta]$, and $k_{obs_{-3}} = k_{-3}[R/S]$. From these values the rate constants $k_1$, $k_2$, $k_3$, $k_{-1}$, $k_{-2}$, and $k_{-3}$ ($M^{-1}\cdot s^{-1}$) characterizing the exchanges between the free ligand *R**/*S** and all the complex isomers expressed by eqs 1−3 were measured and are reported in Table 2.

$$R^*(S^*) + RR\Delta(SS\Lambda) \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} R(S) + R^*R\Delta(S^*S\Lambda) \quad (1)$$

$$R^*(S^*) + RS\Delta(RS\Lambda) \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} R(S) + R^*S\Delta(RS^*\Lambda) \quad (2)$$

$$R^*(S^*) + RR\Lambda(SS\Delta) \underset{k_{-3}}{\overset{k_3}{\rightleftharpoons}} R(S) + R^*R\Lambda(S^*S\Delta) \quad (3)$$

In agreement with the mass action law of equilibria 1−3, the measured $k_1$, $k_2$, and $k_3$ values were found, within experimental error, to equal $k_{-1}$, $k_{-2}$, and $k_{-3}$, respectively.

**Table 3.** Activation Parameters for the Isomerization Processes in $CD_2Cl_2$ Solution of $[Cu(\mathbf{1})_2]PF_6$

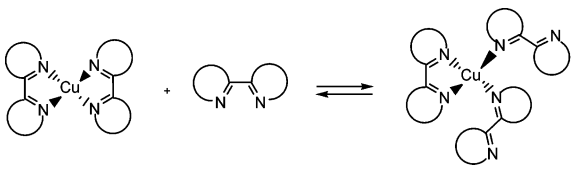
| k | $E_a$[a] | $\Delta H^{\ddagger}$[b] | $\Delta S^{\ddagger}$[c] | $\Delta G^{\ddagger}$[d] (298 K) |
|---|---|---|---|---|
| $k_1$ | 42.4 ± 5.9 | 40.1 ± 5.9 | −74.5 ± 6.5 | 62.3 ± 7.8 |
| $k_{-1}$ | 42.2 ± 8.8 | 39.9 ± 8.8 | −75.9 ± 15.5 | 62.5 ± 13.7 |
| $k_2$ | 37.4 ± 3.8 | 35.0 ± 3.8 | −85.8 ± 12.3 | 60.6 ± 7.4 |
| $k_{-2}$ | 34.8 ± 3.7 | 32.5 ± 3.7 | −94.9 ± 12.3 | 60.8 ± 7.4 |
| $k_3$ | 29.3 ± 5.0 | 27.0 ± 5.0 | −97.9 ± 18.2 | 56.1 ± 10.5 |
| $k_{-3}$ | 35.0 ± 4.5 | 32.7 ± 4.5 | −76.9 ± 11.2 | 55.6 ± 7.9 |
| $k'_1$ | 65.9 ± 3.3 | 63.6 ± 3.3 | −26.4 ± 4.3 | 71.4 ± 2.0 |
| $k'_{-1}$ | 66.0 ± 3.3 | 63.7 ± 3.3 | −26.0 ± 4.5 | 71.5 ± 2.0 |
| $k'_2$ | 71.9 ± 8.9 | 69.5 ± 8.9 | −16.2 ± 26.0 | 74.4 ± 16.6 |
| $k_{-2}$ | 77.4 ± 4.1 | 75.1 ± 4.1 | +28.3 ± 3.5 | 66.7 ± 5.1 |

[a] In kJ·mol$^{-1}$; $E_a = -RT\ln(k/A)$. [b] In kJ·mol$^{-1}$; $\Delta H^{\ddagger} = E_a - RT$. [c] In J·K$^{-1}$·mol$^{-1}$; $\Delta S^{\ddagger} = 1/T(\Delta H^{\ddagger} - \Delta G^{\ddagger})$. [d] In kJ·mol$^{-1}$; $\Delta G^{\ddagger} = -RT\ln(kh/k_BT)$.

As expected for an intermolecular ligand exchange process where the isomers *RS*Λ/*RS*Δ and *RR*Δ/*SS*Λ are very close in energy (present in almost equal amount in solution, 47 and 49%, respectively), the $k_1/k_{-1}$ and $k_2/k_{-2}$ values were found to be of the same order of magnitude. Much faster reaction rates were measured for the intermolecular ligand exchanges with the *RR*Λ/*SS*Δ isomers destabilized by interligand steric interactions and representing only 4% of the reaction mixture. Also, the rate constants $k'_1$, $k'_{-1}$, $k'_2$, and $k'_{-2}$ do not vary with increasing free ligand concentrations (compare values in Tables 1 and 2) as expected for an intramolecular ligand rearrangement process with first-order kinetics.

**Activation Parameters of the Exchange Processes.** From the rate constants measured at 298 and 263 K (Table 2), the activation parameters (i.e. activation energy, enthalpy, entropy, and free energy) of the Λ/Δ intramolecular rearrangements and intermolecular ligand exchanges were determined and are reported in the Table 3.

Two sets of activation parameters emerged from these values, reflecting the two types of exchanges involved at ambient temperature in a $CD_2Cl_2$ solution of $[Cu(\mathbf{1})_2]PF_6$. Free energy values of around 60 kJ·mol$^{-1}$ at 298 K were measured for the intermolecular ligand exchanges, the lowest values of ∼56 kJ·mol$^{-1}$ being associated with the intermolecular ligand exchanges with the destabilized homochiral *RR*Λ/*SS*Δ isomers as might be anticipated. The relatively large negative entropies ranging from −74.5 to −97.9 J·K$^{-1}$·mol$^{-1}$ implies less disorder in the transition states than in the initial one that may reflect an associative mechanism (eq 4) as previously proposed by Van Koten and co-workers for related $[AgL_2]^+$ complexes.[5] In such an associative mechanism, a free ligand may attack a $[CuL_2]^+$ cation to form a four coordinate intermediate, containing one bidentate and two monodentate pyridine−benzimidazole ligands. Dissociation of one of the monodentate bonded ligands may result in ligand exchange.




(4)

The racemization barrier in the heterochiral *RS*Λ/*RS*Δ isomers of $[Cu(\mathbf{1})_2]PF_6$ was measured at around 71 kJ·mol$^{-1}$, a substantially higher value than those previously reported for other $[CuL_2]^+$ cations derived from flexible *o*-substituted diimines such as the 4,4′:6,6′-*p*-tolyl-2,2′-bipyrimidine ($\Delta G^{\ddagger} \sim 61.5$ kJ·mol$^{-1}$ in $CDCl_3$),[4] *o*-substituted-2,2′-bipyridines ($\Delta G^{\ddagger} \sim 56.8-67.4$ kJ·mol$^{-1}$ in $CDCl_3$),[8] and *o*-substituted pyridine imines ($\Delta G^{\ddagger} \sim 58.2-62.5$ kJ·mol$^{-1}$ in $CD_2Cl_2$).[8] The highest configurational stability was observed for $[CuL_2]^+$ salts derived from rigid *o*-substituted-1,10-phenanthrolines ($\Delta G^{\ddagger}$ estimated > 71.8 kJ·mol$^{-1}$ in $CDCl_3$ for the bulky 2-*t*-Bu-1,10-phen).[8] A free energy value at 298 K around 74.4 kJ·mol$^{-1}$ was found for the conversion of the homochiral *RR*Δ/*SS*Λ isomers into their *RR*Λ/*SS*Δ. Meaningful comment on this value is difficult as it is associated with a relatively large error margin due to the low *RR*Λ/*SS*Δ concentration leading to a large standard deviation for $k_2$ (Table 2). Nonetheless, it appears that the lowest free energy ($\Delta G^{\ddagger} \sim 66.7$ kJ mol$^{-1}$) was obtained for the reverse reaction, e.g. for the conversion of the less stable *RR*Λ/*SS*Δ isomers to the more stable *RR*Δ/*SS*Λ.

## Conclusions

The kinetics of isomerizations of homo- and heterochiral $[Cu(\mathbf{1}-\mathbf{3})_2]PF_6$ complexes in $CD_2Cl_2$ solutions were studied at different mixing times and temperatures by 2D exchange proton NMR spectroscopy. Two-dimensional NMR exchange spectroscopy appeared as a powerful tool for the quantification of chiral ligand rearrangements and exchanges in $[CuL_2]^+$ cations, provided that the exchanging species are clearly resolved in the NMR spectrum and the time scale of the process is shorter than the spin−lattice relaxation time. Both conditions were almost ideally met by $[Cu(\mathbf{1})_2]PF_6$ in $CD_2Cl_2$ solution providing a unique access to the kinetic and activation parameters of the chiral diimine exchanges in the $[CuL_2]^+$ cations. The Λ/Δ isomerizations in $[Cu(\mathbf{1}-\mathbf{3})_2]^+$ cations were shown to occur through an intramolecular ligand rearrangement. Racemization in the heterochiral enantiomers *RS*Λ/*RS*Δ took place at ambient temperature in $CD_2Cl_2$ on a time scale of about 1.9, 4.4, and 0.3 s$^{-1}$ for $[Cu(\mathbf{1})_2]^+$, $[Cu(\mathbf{2})_2]^+$, and $[Cu(\mathbf{3})_2]^+$, respectively. The rates of ligand flipping around the copper ion were very sensitive to the bulkiness of the phenyl substituents of the benzimidazole ring but also to the stabilizing interligand $\pi-\pi$ stacking interactions such as those developing in $[Cu(\mathbf{1})_2]^+$. For the homochiral complexes the conversion of the most stable *RR*Δ/*SS*Λ isomers of $[Cu(\mathbf{1})_2]^+$ into their *RR*Λ/*SS*Δ diastereoisomers occurs on a time scale of about 0.6 s$^{-1}$. A rate 20 times faster was measured for the reverse reaction according to the destabilization of the *RR*Λ/*SS*Δ isomers by strong steric interligand interactions. Much slower intermolecular ligand exchanges implying free ligand have been clearly evidenced at ambient temperature in $CD_2Cl_2$. The free energies at 298 K for the Λ/Δ isomerizations in $[Cu(\mathbf{1})_2]^+$ cations range from 66.7 to 71.4 kJ mol$^{-1}$, while lower values ranging from 55.6 to 62.5 kJ mol$^{-1}$ were determined for the intermolecular ligand exchanges. The negative and relatively large entropy values found for the intermolecular ligand

exchanges suggest an associative mechanism as previously proposed for related $[AgL_2]^+$ cations.[5]

## Experimental Section

**General Considerations.** The ligands **1**−**3** and the complexes $[Cu(\mathbf{1}-\mathbf{3})_2]PF_6$ were synthesized as previously described.[9] Deuterated dichloromethane was purchased from Eurisotop. The 2D $^1$H EXSY NMR spectra were recorded in $CD_2Cl_2$ solution (450 $\mu$L) at the following concentrations: 24.5 mM for $[Cu(\mathbf{1})_2]PF_6$; 46.4 mM for $[Cu(\mathbf{2})_2]PF_6$; 43.5 mM for $[Cu(\mathbf{3})_2]PF_6$. Both solutions were dried by adding crushed molecular sieves to remove a large proportion of water.

The 2D $^1$H EXSY NMR spectra were performed at 400.13 MHz on a Bruker DPX apparatus equipped with an inverse broad band probe of 5 mm diameter and were recorded in the phase sensitive mode with time proportional phase incrementation,[13] using the well-known three 90° pulse sequence of Jeener et al.[14] The spectral width was adapted so that only the resonances of the H1 methyl protons of $[Cu(\mathbf{1}-\mathbf{3})_2]PF_6$ were observed (around 400 Hz, between 1 and 2 ppm using TMS as reference). The recycling delay was 1.8 s. The 90° length (6.5 $\mu$s) was calibrated for all samples before the experiments. The initial (t1, t2) matrixes of 256 × 1024 real data points were zero-filled to 1024 × 1024 to give a final resolution close to 1 Hz/point in each of the two dimensions. The number of scans used was 8. For all compounds 10−13 experiments were recorded at 298 K with mixing times $\tau_m$ ranging from 0 to 500 ms. The auto- and cross-peak volumes were determined after phase and baseline correction of the two dimensions using the Bruker UXNMR software.

**Rate Constant Calculations.** Two methods, as previously described, were used.[10a] First, the initial rate method with normalization of the cross-peak volume $V_{ij}(t_m)$ to the auto-peak volume $V_{jj}(t_m)$ was used to discriminate one-step (direct) and multistep (relayed) exchanges.[10b] The exchange matrix resolution method of Perrin, Gipe, and Dwyer[12] allows the determination of the rate constant from a single experiment recorded at one mixing time by resolving the exchange matrix $\mathbf{L} = (1/t_m) \ln \mathbf{A} = (1/t_m)\mathbf{U}(\ln \lambda)\mathbf{U}^{-1}$, where the elements of the experimental matrix **A** are such that $A_{ij} = V_{ij}(t_m)/M_{0j}$ and $A = U\lambda U^{-1}$, where $M_{0j}$ is the volume of the corresponding auto-peak measured at $t_m = 0$ and $U$ and $\lambda$ are respectively the eigenvector and eigenvalue matrixes of **A**. The resolution of all the matrixes was done by using the "Mathcad 2000 professional" software. The rate constant obtained for each temperature was averaged from the data obtained at different mixing times and given with its standard deviation.

**Acknowledgment.** We thank the University of Bordeaux 1, the CNRS, and la Région Aquitaine for financial support.

**Supporting Information Available:** $^1$H NMR spectra of $[Cu(\mathbf{1}-\mathbf{3})_2]PF_6$ recorded in $CD_2Cl_2$ at 298 K and buildup curves for $[Cu(\mathbf{2})_2]PF_6$ and $[Cu(\mathbf{3})_2]PF_6$. This material is available free of charge via the Internet at http://pubs.acs.org.

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