Atropisomer and Diastereomer Generation and Control in Ruthenium Bis(bipyridine) Phosphonite Complexes

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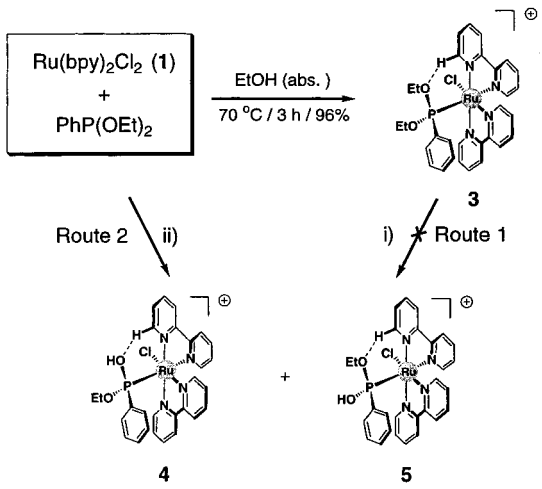
The facile generation, control, and induction of chirality is of current prominent interest in the scientific community.[1] With the increasing realization that these aspects are key factors in numerous bioprocesses, it has been recognized that the effective generation and control of chirality is crucial to the future progress in many areas.[2] Atropisomerism, in which chirality is generated by the formation of two or more stable (non-interconverting) rotational isomers, is a potentially powerful and versatile tool for many new "chemical" technologies. The ability to "write" and "read" chiral information, in principle, may be applied to nanoscale information storage and retrieval devices, chiral sensors, optoelectronics, and asymmetric and biomimetic catalysts among others. However, because of difficulties in rationally generating and controlling atropisomerism, with the exception of asymmetric catalysis,[3] it has not yet been applied to such challenging areas, although it has great potential. Photochromic generation, control, and detection of atropisomerism is particularly attractive, providing a facile, non-destructive approach to the generation of a number of "chiral states". The stereochemistry of ruthenium bis(bipyridine) compounds already plays a proven important role in many areas of fundamental and applied chemistry; with specific areas of current interest being catalysis,[4] stereoselective energy/electron transfer,[5] optoelectronics, and molecular devices.[6] With the above considerations in mind we have recently been working toward the rational generation, control, and detection of chirality in ruthenium bis(bipyridine) complexes.

We previously reported a simple methodology for the controlled sequential addition of different bipyridine units to the ruthenium center in a racemic[7] or asymmetric[8] fashion. In addition we have demonstrated a new methodology for the chiral discrimination of ruthenium bis(bipyridine) derivatives starting from racemic Ru(bpy)$_2$Cl$_2$ (**1**) using enantiomerically pure sulfoxide ligands.[9] Recently we obtained experimental evidence to suggest that for *cis*-[Ru(bpy)$_2$(PhP(OMe)$_2$)(Cl)]$^+$ (**2**), irradiation at the LC (293 nm) and MLCT bands (400−430 nm) resulted in the reversible conformational switching of the PhP(OMe)$_2$ moiety around the Ru−P bond,[10] thus indicating atropisomeric conformer conversion hitherto unreported, can be induced by the electronic interaction between the delocalized π system of the bipyridine groups and the d-orbitals of the ruthenium metal.

Scheme 1[a]



[a] *Reagents and conditions*: i) EtOH (85−50%), 70 °C, 20 h or EtOH/H_2O (85:15 v/v), pH < 1.5, 70 °C, 6 h; ii) EtOH/H_2O (85:15 v/v), 70 °C, 20 h.

X-ray diffraction analysis of **2**·PF_6[10] has shown the two adjacent OMe groups to be in distinct chemical environments, a feature fully supported by solution NMR studies. We realized that this should lead, via differential OMe group substitution,[11] to the unique chirogenesis of a new class of ruthenium bis(bipyridine) diastereomers with inherent diastereomeric excess (de) generated from achiral materials, a feature not previously reported for ruthenium bis(bipyridine) compounds. To enhance that stability of the ground-state conformation of **2** we modified the P(OMe)$_2$ fragment to employ more bulky substituents, to hinder the possible thermal rotation around the Ru−P bond that would otherwise racemize the chiral OMe positions, thus losing any inherent de from the substitution reaction.

In this present work we report the synthesis and photochemistry of the ethoxy analogue *cis*-[Ru(bpy)$_2$(PhP(OEt)$_2$)(Cl)]$^+$ (**3**) and related compounds. The conformation of the phosphonite ligand relative to the ruthenium center was established, from X-ray diffraction analysis,[10] to be almost equivalent to that of **2**, having spatially distinct OEt groups. The conformation found in **3**, as in **2**, is stabilized by $\pi-\pi$ interactions ($\sim$3.5 Å) between the ligand phenyl ring and a pyridine ring and a C$_{(py)}$−H···OEt (2.32 Å) intramolecular hydrogen bond.

Scheme 1 outlines the experimental methodology and compounds used in this work. The attempted displacement of one OEt substituent by OH in a simple hydrolytic reaction, to our surprise, failed even under harsh reaction conditions (Route 1). Consequently, the in situ ligation/substitution approach (Route 2) was adopted, and this led to the development of a new synthetic method for a potentially highly important class of ruthenium bis(bipyridine) diastereomers, in which the preferred diastereomer

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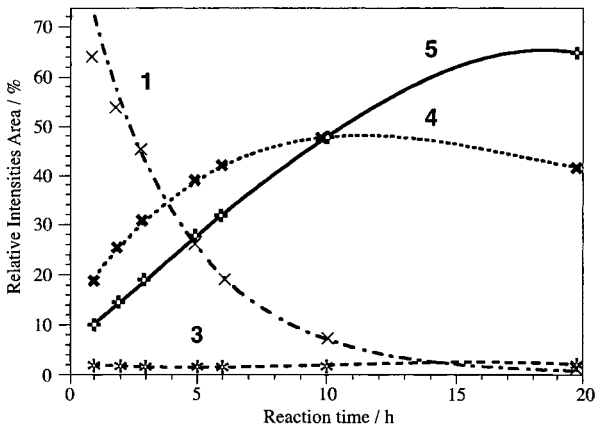


Figure 1. Plot of HPLC peaks relative intensities (area %) of **1**, **3**, **4**, and **5** as a function of reaction time at 70 °C in EtOH/H_2O (85:15 v/v) solution.

and to an extent the de could be controlled by the reaction conditions. The reaction forms two main and one minor product. Figure 1 shows the variation in the increase of the reaction products **3**, **4**, and **5**, and corresponding decrease of the starting material $Ru(bpy)_2Cl_2$ (**1**) with time.

Initially products **3**, **4**, and **5** are formed with relative intensities 6:62:32, with **4** existing in 32% de. As the reaction proceeds the intensity of **3** remains constant, while **4** and **5** increase in intensity. However, at longer reaction times an inversion in the relative peak intensities (and thus de) of **4** and **5** occurs, resulting in **5** as the final major product with 22.4% de. From these results it is clear that by varying the reaction time we can control the preferred diastereomer, and to a degree the de.

Subsequent X-ray diffraction analysis revealed these products to be: the bis-ethoxy derivative *cis*-Δ/Λ-[$Ru(bpy)_2(PhP(OEt)_2)$-(Cl)]Cl (**3**), and the new type of diastereomerics Δ-(*R*)- and Λ-(*S*)-[$Ru(bpy)_2(PhP(OH)(OEt))(Cl)$]Cl (**4**), Δ-(*S*)- and Λ-(*R*)-[Ru-$(bpy)_2(PhP(OEt)(OH))(Cl)$]Cl (**5**), in the ratio 2:38:60. The absolute configurations at the phosphorus centers are determined relative to those of the ruthenium center. The different NMR spectra of **4** and **5** unambiguously confirm their diastereomeric relationship, with the most upfield chemical shifts of the aromatic protons of the phosphonite phenyl group at ∼7.0 ppm and ∼6.5 ppm for **4** and **5**, respectively, in good agreement with our previous results for ruthenium bis(bipyridine) diastereomers utilizing chiral sulfoxide ligands.[7b]

By (bench) column chromotography performed in the dark the products were isolated, allowing investigation of photoinduced atropisomer formation. Crystals of **3**, **4**, and **5** (Figure 2) were grown from a $MeOH/CH_3CN/Et_2O$ mixed solvent in the dark. Derivative **4** was also periodically irradiated during crystallization at the LC band (295−305 nm) (Scheme 2) to induce the proposed atropisomer formation, via the electronic interaction between the delocalized π system of the bipyridine groups and the d-orbitals of the ruthenium metal, forming **6**, which was identified by X-ray crystal structure determination as a new diastereomeric atropisomer. The structures of **4**, **5**, and **6** show different orientations of the PhP(OEt)(OH) moiety with respect to the complex's Ru-$(bpy)_2Cl$ core. All structures crystallize in centrosymmetric spacegroups and we describe the Δ stereoisomers.

In **4** (see Figure 2) the phosphorus is in the *R* configuration, and the conformation is intramolecularly stabilized by a C−H···OH hydrogen bond and $\pi-\pi$ overlap between the ligand phenyl group and a pyridine ring. In addition there is a methanol solvent molecule which forms an intermolecular acceptor hydrogen bond to the OH group of one molecule and a donor hydrogen bond to the chlorine of a second molecule. In **5** the phosphorus is *S*, and the conformation is stabilized by a C−H···OEt hydrogen bond

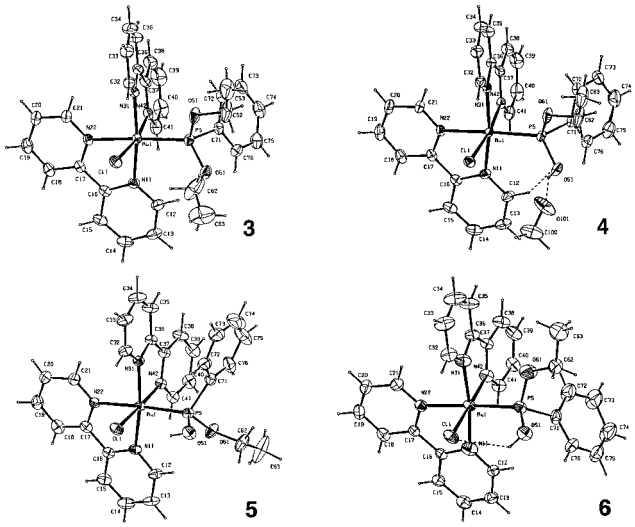
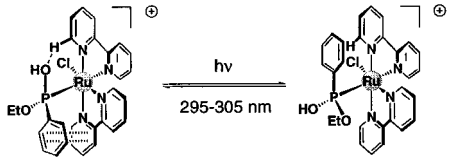


Figure 2. Ortep view of molecules **3**·PF_6, **4**·PF_6, **5**·PF_6, and **6**·PF_6 with thermal ellipsoids at 30% probability.

Scheme 2. Photochromic Atropisomeric Induction



and $\pi-\pi$ overlap between the ligand phenyl group and a pyridine ring; further, the conformation found in **5** is additionally stabilized by a strong intramolecular O−H···Cl hydrogen bond (O···Cl 3.05 Å, O−H···Cl 1.44 Å, H···Cl 2.30 Å). **6** (See Figure 2) is obtained from **4** by photoexcitation at the LC band and the *R* configuration is maintained. However, a rotation of the phosphonite ligand around the Ru−P bond of 41° has occurred resulting in a structure with neither C−H···O hydrogen bond nor $\pi-\pi$ overlap, although a O−H···Cl hydrogen bond is now formed.

In conclusion we have developed the first chirally discriminating methodology for deriving ruthenium bis(bipyridine) diastereomers from achiral starting materials and reagents in appreciable de. This method takes advantage of the stabilization of specific chiral molecular conformations via a cooperative network of weak intramolecular $\pi-\pi$ interactions and $C_{(py)}$−H···O and O−H···Cl hydrogen bonds; demonstrating that the application of so-called "weak" interactions can result in a high degree of structural control. Further, photoexcitation of diastereomer **4** resulted in a photochromic rotation of the PhP(OH)(OEt) moiety to form **6**; thus the formation of a diastereomeric atropisomer couple has been achieved, with the unprecedented feature that both structures have been obtained by X-ray analysis so that the differences in conformation can be confirmed. The ground-state structure **4** is stabilized by intramolecular $\pi-\pi$ and $C_{(py)}$−H···O interactions, with the high energy atropisomer forming no such contacts, only a O−H···Cl hydrogen bond.

The set of chiral compounds reported in this work are highly unusual, as the molecules possess three levels of chirality (Δ and Λ at the ruthenium center, P-centered (*R* and *S*), and atropisomeric) all of which can be generated from achiral materials, and to a degree controlled via appropriate reaction conditions.

Supporting Information Available: ^1H and ^{13}C NMR spectra for **3**, **4**, **5**, and **6**, HPLC chromatogram charts. X-ray crystallographic files (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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