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Metallaaromatic Biaryl Atropisomers

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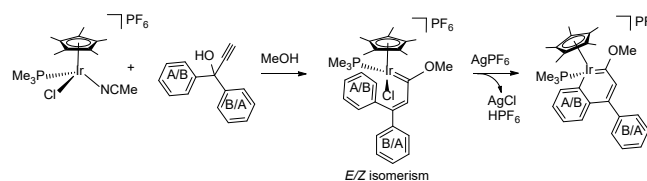
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Synthesis of stable irida-binaphthyl and -phenanthryl complexes, the first examples of metallaaromatic biaryl atropisomers, has been achieved. The combination of experimental and theoretical studies revealed that the nature of these systems is comparable to that of well-known 1,1'-binaphthalene both in terms of aromaticity and atropisomerism.

Many chemists have been fascinated by the replacement of a C–H moiety by a transition-metal atom in aromatic rings.¹ Studies in this intriguing field of metallaaromatic compounds have given rise to new topologies such as pentalenes, and -pentalynes² or metallacyclic systems with fused rings,³ and from a fundamental point of view have been mostly focused on metalla-benzenes^{4, 5} and -benzynes.^{6, 7} Larger siblings, such as metalla-naphthalenes, -naphthalynes,⁸ and -anthracenes,^{9, 10} are more rare and merely evidence of unstable metallaphenanthrenes were found.^{11, 12} However, although optically active organometallic compounds with chiral transition-metal atoms are well explored,^{13–15} and have a great impact in catalytic applications,¹⁶ no studies have been performed to explore axial chirality in metallaaromatic systems. Stereoisomers arising from hindered rotation about a single bond, known as atropisomers, are abundant among organic systems with great relevance in drug discovery,¹⁷ asymmetric catalysis,¹⁸ and molecular switches.¹⁹ On the contrary, only very few examples of their organometallic counterparts^{20, 21} have been reported and no metal-bearing biaryl systems presenting atropisomerism have been found to date. In this regard, we have recently developed a methodology for the synthesis of

iridanaphthalene complexes upon reaction of [IrCp*Cl(NCMe)(PMe₃)]PF₆ with diarylpropargyl alcohols providing methoxyalkenylcarbeneiridium complexes (Scheme 1).^{22, 23} The *E/Z* isomerism in these intermediates determines the final structure of the resulting iridanaphthalene since the C–H activation takes place over the aromatic ring nearest to the metal center.



Scheme 1. General methodology for the synthesis of iridanaphthalene complexes. The atropisomeric character in iridanaphthalene complexes may lead to diastereoisomeric mixtures due to the presence of a metal chiral center. The possible stereogenic information in alcohols is lost due to the planarization of the quaternary carbon atom during its transformation.

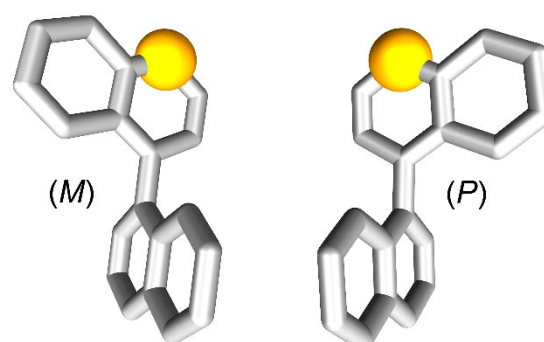


Figure 1. General representation of the two atropisomers of a metallaaromatic binaphthyl and stereogenic descriptors for the axial chirality.

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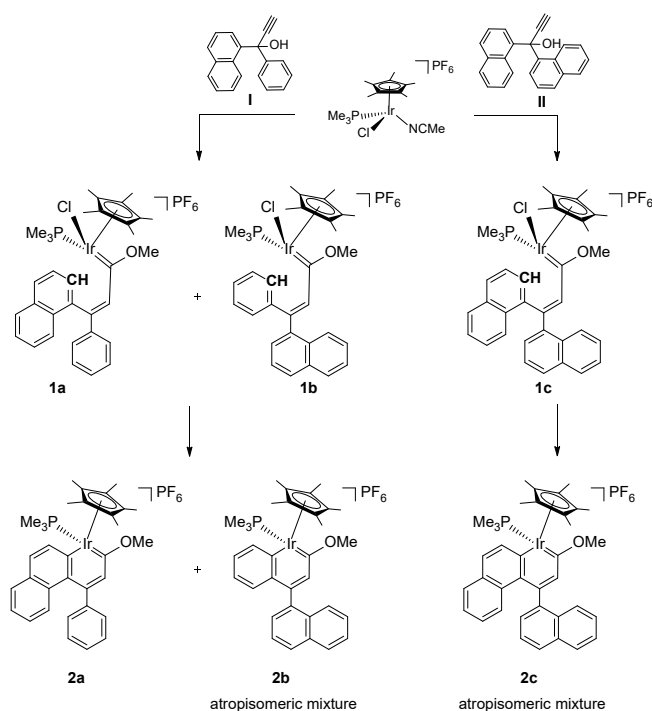
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Binaphthalene derivatives are the most representative of classical organic atropisomeric systems because of their valuable applicability, with for instance BINAP and BINOL extensively used in asymmetric catalysis.²⁴ Remarkably, even when the exchange of C atoms by transition metals may significantly expand the scope from purely organic aromatic rings, metallated analogs of atropisomeric biaryls are still unknown (Figure 1). The study presented herein represents a proof of principle for metallaaromatic biaryl atropisomers with the synthesis, characterization, and theoretical analysis of the first examples of this compound class.

Taking advantage of the versatility of our methodology,^{22, 23} we performed the reaction of naphthyl phenyl propargyl alcohol **I** with [IrCp*Cl(NCMe)(PMe₃)]PF₆ (Scheme 2, for more information see the ESI), which led to a mixture of methoxyalkenylcarbeneiridium complexes **1a** and **1b** in good yield. Subsequent C–H activation of the aromatic ring closer to the metal center yielded iridaphenanthrene **2a** and iridanaphthalene **2b**, respectively.



Scheme 2. Synthesis of iridaphenanthrenes **2a** and **2c** and iridanaphthalene **2b**.

A thorough investigation of the nuclear magnetic resonance (NMR) and high-resolution mass spectrometry (HR-MS) data of the reaction mixture supported the presence of **2a** and **2b** (17:83 mole ratio estimated by NMR, respectively, for more information see the ESI)²⁵. Notably, while iridaphenanthrene **2a** shows a single set of signals in the NMR spectra, duplicated signals corresponding to iridanaphthalene **2b** evidence the presence of two diastereoisomers in a 64:36 mole ratio. This phenomenon can be explained due to the simultaneous presence of the iridium chiral center and hindered rotation about the biaryl bond leading to atropisomerism. To turn off the presence of more than one metallaaromatic topology arising

from *E/Z* isomerism of methoxyalkenylcarbene intermediate **1**, we used propargyl alcohol **II** featuring two identical naphthyl moieties, which therefore leads solely to methoxyalkenylcarbeneiridium complex **1c**. The following C–H activation of **1c** gave iridaphenanthrene **2c**. The NMR and HR-MS data confirmed the proposed structure. Additionally, observation of duplicated signals in the NMR spectra reveals the presence of two atropisomers in a 56:44 mole ratio (for more information see the ESI).

Computed relaxed potential energy surface about the biaryl bond in **2b** and **2c** at the Hartree–Fock level of theory provided rotational barriers of 28.0 kcal mol⁻¹ and 22.7 kcal mol⁻¹ respectively.²⁶ These values are comparable to the calculated for 1,1'-binaphthalene, with an experimental racemization half-life of 14.5 min at 50 °C,²⁶ at the same level of theory (for more details, see the ESI) and consistent with the experimental observation of atropisomerism by means of NMR in **2b** and **2c** at room temperature. Measurement of experimental rotational barriers by means of NMR was hampered by the low solubility of **2b** and **2c** in reliable solvents. The geometry of diastereoisomers (*S,P*) and (*S,M*) for **2b** and **2c** was optimized at the DFT level of theory employing Gaussian09 (for more details, see the ESI).^{26, 27} The calculated energy differences between (*S,M*)-**2b** and (*S,P*)-**2b** and between (*S,M*)-**2c** and (*S,P*)-**2c** of 0.92 kcal mol⁻¹ corresponding to a 78:22 ratio and 0.35 kcal mol⁻¹ corresponding to a 56:44 ratio respectively, are in good agreement with the ratios observed experimentally by NMR. Two dimensional NMR experiments were performed to get more insight into the structure of these new topologies. {¹H,¹H} NOESY NMR experiment on **2c** shows correlations between C²H (7.02 ppm) and C⁸H (8.27–8.17 ppm) for one of the atropisomers (Figure 2, black lines), while featuring correlations between C²H (7.07 ppm) and C²H (7.72–7.56 ppm) for the other (Figure 2, black dashed lines). Cross-checking these observations with the predicted conformation of the biaryl system in (*S,P*)-**2c** with a 127.9° torsion angle and the predicted conformation of the biaryl system in (*S,M*)-**2c** with a –56.1° torsion angle enables the relative configuration assignment of the two atropisomers.

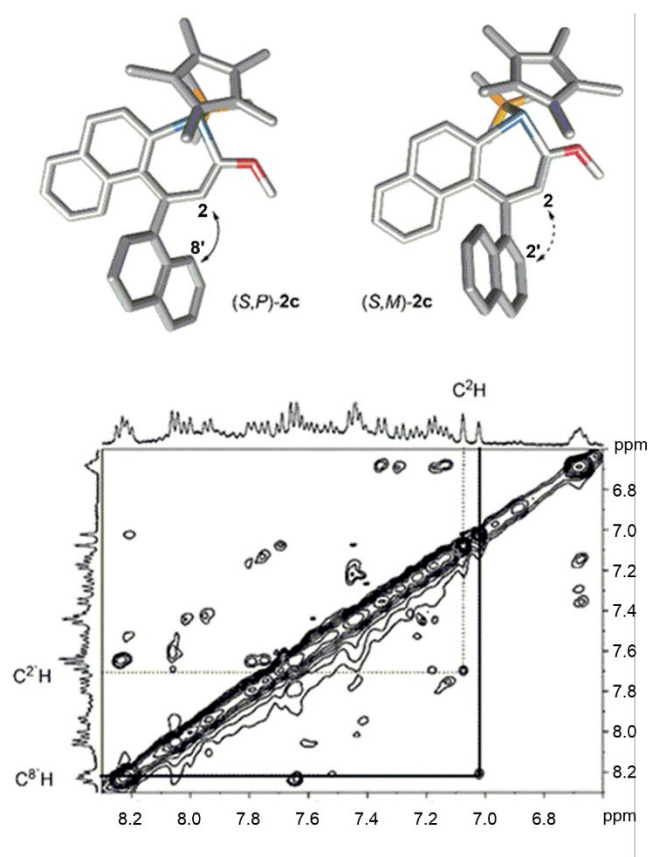


Figure 2. The $\{^1\text{H},^1\text{H}\}$ NOESY NMR experiment confirms the spatial arrangement of (S,P) -**2c** (black lines) and (S,M) -**2c** (black dashed lines).

In order to analyse the aromaticity of the obtained structures, the anisotropy of the current-induced density (ACID) method was employed. This method, developed by Herges and Geuenich, is based on magnetic properties and allows the visualization of the ring current formed when a magnetic field is applied.²⁸ The ACID isosurfaces for (S,M) -**2c** and (S,P) -**2c** feature similar aromaticity as seen for the purely organic analog 1,1'-binaphthalene with CIV value 0.071 (Figure 3, for more details, see the ESI). To give a numerical value to delocalization effects, we predicted the critical isosurface values (CIV, value of the isosurface at which the topology of the conjugation changes from cyclic to noncyclic). In the case of **2c**, the CIVs between the Ir and C atoms are 0.052 and 0.044 for (S,M) -**2c** and (S,P) -**2c**, respectively. These values reveal a clear aromatic character for the two atropisomers and is comparable with the values for iridabenzene complexes (0.047, for more information see the ESI).²⁹

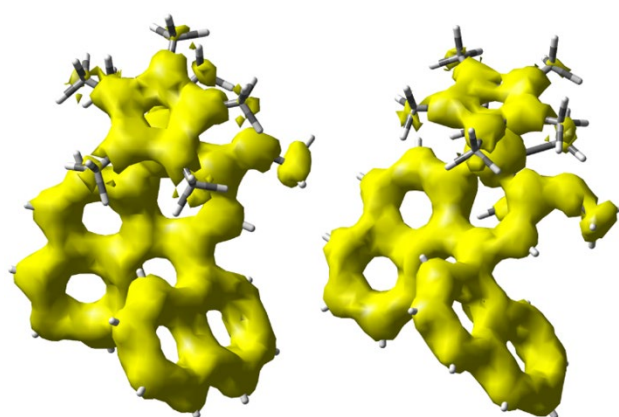


Figure 3. ACID plots for (S,M) -**2c** (left) and (S,P) -**2c** (right) with an isosurface value of 0.052 and 0.044 respectively.

In conclusion, metallaaromatic biaryl atropisomers were obtained and theoretically studied for the first time. Furthermore, relative configuration assignment of atropisomeric diastereoisomers was possible by $\{^1\text{H},^1\text{H}\}$ NOESY NMR and theoretical analysis. On the other hand, the synthesis, isolation, and characterization of stable iridaphenanthrene complexes presented herein has no precedent and provides evidence for the versatility of our synthetic methodology of giving access to larger polycyclic metallaaromatic systems. The aromatic character along with the stability and atropisomeric nature of these compounds represent the birth of metallaaromatic biaryl atropisomers. New analogs with larger rotational barriers to fully explore the potential of this new family of aromatic compounds are in progress.

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Conflicts of interest

There are no conflicts to declare.

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