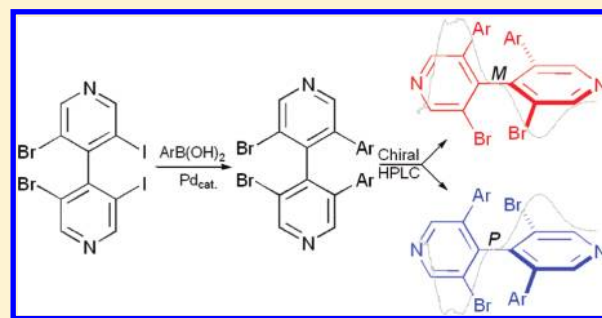


Synthesis, Resolution, and Absolute Configuration of Chiral 4,4'-Bipyridines

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S Supporting Information

ABSTRACT: A chiral polyhalogenated 4,4'-bipyridine derivative is described allowing an easy access to a new family of chiral 4,4'-bipyridines by site-selective cross-coupling reactions. The absolute configurations of all the HPLC separated enantiomers were determined by X-ray diffraction and electronic circular dichroism coupled with time-dependent density functional theory calculations.

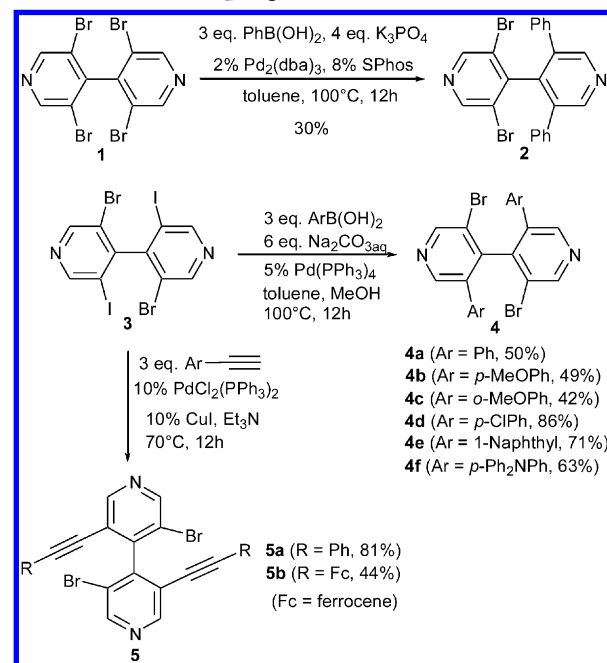


4,4'-Bipyridine is one of the most famous ligands used in supramolecular chemistry due to the presence of two donor atoms along a rigid structure.¹ Moreover, it is an excellent building block for the preparation of viologens² and liquid crystals.^{3,4} Considering the importance of chiral supramolecular networks in many applications such as asymmetric catalysis,⁵ it was surprising to find limited examples of chiral 4,4'-bipyridines in the literature.^{6–8}

We have recently described a simple method to access to the 4,4'-bipyridine scaffold possessing several halogen groups.⁹ Herein, we described a new chiral polyhalogenated 4,4'-bipyridine easily functionalized by cross-coupling reactions. The configurationally stable enantiomers were separated on chiral HPLC columns and their absolute configuration was assigned on the basis of X-ray diffraction (XRD) and electronic circular dichroism (ECD) analyses coupled with time-dependent density functional theory calculations (TD-DFT).

With the aim to prepare atropisomeric 3,3',5,5'-tetrasubstituted 4,4'-bipyridines, the reactivity of 3,3',5,5'-tetrabromo-4,4'-bipyridine **1** and 3,3'-dibromo-5,5'-diiodo-4,4'-bipyridine **3** was investigated under the Suzuki reaction conditions.¹⁰ Starting from **1**, it was observed the formation of the 3,5-disubstituted-3',5'-dibromo-4,4'-bipyridine **2**, as main product.¹¹ This result suggested an electronic effect induced onto the mono phenyl substituted pyridine ring by the first introduced phenyl moiety which makes the position 5 more reactive than the positions 3' and 5'. Differently, in **3**, the iodine onto the 3,3' position acts as a regioselective modulator of reactivity pivoting the substitution onto the iodine substituted C atoms of the 4,4'-bipyridine system and, consequently, leading to the formation of novel chiral 4,4'-bipyridines **4a–f** (Scheme 1).¹² Similarly, alkynyl-substituted derivatives **5** were obtained through a

Scheme 1. Cross-Coupling Reactions of 3



Sonogashira reaction.¹³ All prepared compounds bear on the *ortho-ortho'* positions of the heterocyclic scaffold two π -electron groups.

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All of the atropisomeric 3,3',5,5'-tetrasubstituted bipyridines were enantioseparated by chiral HPLC. The use of this technique was previously reported by Schalley and co-workers for the separation of three chiral bis-amide substituted bipyridines on an immobilized Chiralcel OD column.⁶ For our compounds, polysaccharide-based columns proved also to be versatile. For instance, bipyridines **3** and **4b** were separated on Lux Cellulose-2 and Chiralcel OD-H columns, respectively.¹⁴ After multimilligram recovery of the enantiomers,¹⁵ assignment of absolute configurations for **3** and **4b** were achieved by single crystal XRD analysis, using anomalous dispersion due to the presence of heavy atoms in the structures (Figure 1).

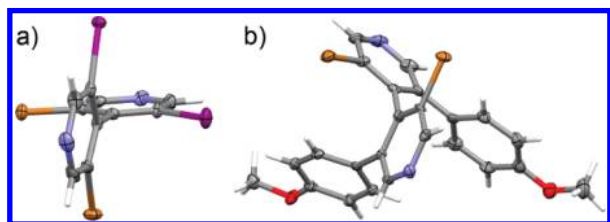


Figure 1. ORTEP plots of one of the four molecules within the asymmetric units of (a) **3** and (b) **4b**. Thermal ellipsoids set at 50% probability and hydrogen atoms shown as sticks. The absolute configurations are *P* for **3** and *M* for **4b**.

For **3** (2nd eluted peak) enantiomer, the Flack parameter refined to 0.124(5); this small value identifies the configuration of **3** as *P*, but also shows that a minor amount of *M* enantiomer is also present in the investigated sample as an enantiomorphous crystal phase (see the Supporting Information for full refinement details). It has to be noted that the enantiomeric excess after the chiral HPLC separation was 97.8%, already evidencing a small enantiomeric contamination. In the case of **4b** (1st eluted peak) and **5b** (second eluted peak) enantiomers, the low value of the Flack parameters (respectively $-0.005(5)$ and $-0.021(6)$) and of their standard uncertainties unambiguously identify the absolute configurations of **4b** (1st eluted peak) as *M* and of **5b** (second eluted peak) as *P* (see the Supporting Information for ORTEP view of (*P*)-**5b**).

Because all compounds could not be crystallized (e.g., **5a** forms an oil at room temperature), ECD spectroscopy was then used in order to determine the absolute configuration of all enantiomers of bipyridines **4**–**5** (Figure 2). The ECD signal for compound **5b** was weak and is therefore omitted in Figure 3 for clarity (see the Supporting Information for ECD spectrum of **5b**).

Assignment of absolute configurations was then performed by comparing the experimental spectra to the data calculated at the TD-DFT level of theory (CAM – B3LYP/6-311+G(d,p)) using the Gaussian09 program package¹⁶ (Figure 3 and Supporting Information).

Except for the ferrocenyl compound **5b** for which no reasonable ECD spectra could be calculated, the agreement between experimental and theoretical ECD spectra were good. The main discrepancy is a systematic shift of the calculated spectra to shorter wavelengths, as evidenced in previous studies using the same DFT functional.¹⁷ These comparisons thus allow a clear identification of the absolute configurations for all the recovered enantiomers, as collected in Table 1. In particular, the absolute configuration found by ECD for **4b** is coherent with the one assessed through the XRD analysis.

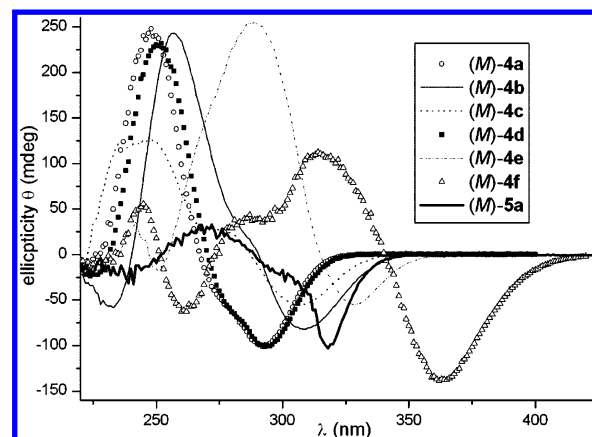


Figure 2. Experimental ECD spectra for compounds (*M*)-**4** and (*M*)-**5a** (298K, MeOH, 0.1 mM, 1 cm cells).

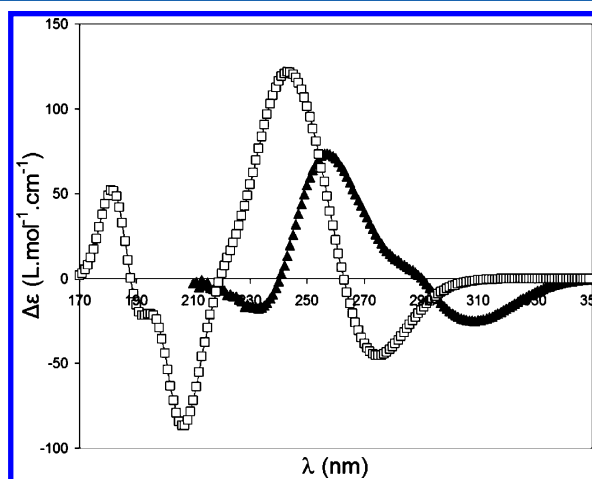


Figure 3. Comparison of experimental (black triangles) and theoretical (squares) ECD spectra for the (*M*)-**4b** enantiomer.

Table 1. Absolute Configurations of All Bipyridine Atropisomers

bipyridine	HPLC column	absolute configuration (ee%)	
		first eluted peak	second eluted peak
3	Lux Cellulose-2	<i>M</i> (>99)	<i>P</i> (97.8)
4a	Lux Cellulose-4	<i>M</i> (>99)	<i>P</i> (96.0)
4b	Chiralcel OD-H	<i>M</i> (>99)	<i>P</i> (>99)
4c	Lux Cellulose-4	<i>M</i> (>99)	<i>P</i> (>99)
4d	Lux Cellulose-1	<i>P</i> (97.7)	<i>M</i> (96.2)
4e	Lux Cellulose-4	<i>M</i> (>99)	<i>P</i> (>99)
4f	Lux Cellulose-4	<i>M</i> (>99)	<i>P</i> (>99)
5a	Lux Cellulose-2	<i>M</i> (92.0)	<i>P</i> (94.0)
5b	Lux Cellulose-2	<i>M</i> (95.0)	<i>P</i> (95.0)

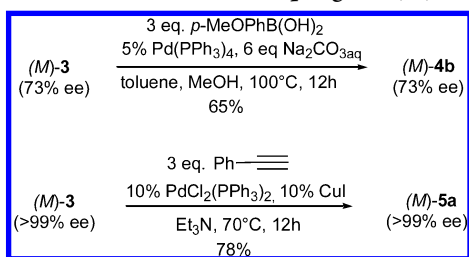
From Figure 2 it could be noticed that for all enantiomers of the same absolute configuration *M* (respectively *P*), the ECD spectrum presents first a negative (respectively positive) Cotton effect at high wavelengths then a positive (respectively negative) Cotton effect at lower wavelengths. This is even the case for **5b** for which no reasonable ECD spectra could be calculated and for which the absolute configuration was assessed through XRD only.

For both *P,M* enantiomers of **4b**, no racemization was observed after heating in methanol at 70 °C for 72 h, suggesting

a high barrier for racemization. Indeed, activation energy barriers calculated at the DFT level of theory (using the B97D functional including dispersion corrections) for bipyridines **3**, **4a–e**, and **5a** are all over 160 kJ/mol. In other words, the lowest racemisation temperature (T_r , temperature at which the half-life time of the atropisomer is 1000 s) is 383 °C, obtained for **4c** (for details, see the Supporting Information). It is then expected that all these new chiral bipyridines can retain their chiral configurations over a long period of time, in particular the tetrahalogenated bipyridine **3** ($T_r = 536$ °C).

The use of bipyridine **3** as an enantiomerically pure precursor was then considered by studying the transfer of the stereochemical information after cross-coupling reactions. Such study on binaphthyl derivatives have shown stereoconservation or racemization depending on the organometallic counterpart (Mg, Zn, Sn, B, Al) and the reaction conditions.^{18–23} In our case, complete stereoconservativity was observed after Suzuki and Sonogashira couplings with bipyridine (*M*)-**3** demonstrating that bipyridine **3** is configurationally stable under palladium catalysis (Scheme 2). This result indicates that both

Scheme 2. Stereoconservative Couplings of (*M*)-**3**



enantiomers of **3** can be used for the direct preparation of enantiomerically pure 4,4'-bipyridines.

In summary, we have presented a novel family of chiral configurationally stable 4,4'-bipyridines. For all compounds, the absolute configurations of the enantiomers were assigned on the basis of XRD and ECD analyses. The ease of introduction of different substituents on the parent 3,3'-dibromo-5,5'-diiodo-4,4'-bipyridine **3** makes this compound an essential precursor toward enantiomerically pure 4,4'-bipyridine ligands for incorporation in metal–organic frameworks (MOFs).

EXPERIMENTAL SECTION

General Experimental Methods. All reactions were performed under an atmosphere of argon in oven-dried glassware. Diisopropylamine was distilled over CaH₂. Tetrahydrofuran (THF) and toluene were distilled over sodium/benzophenone and stored over sodium. All other solvents and reagents were used as received. TLC was performed on silica gel plates and visualized with a UV lamp (254 nm). Chromatography was performed on silica gel (70–230 mesh). All melting points were uncorrected. The ¹H and ¹³C NMR spectra were recorded at 200 and 50 MHz or at 250 and 66 MHz, respectively. Chemical shifts are quoted in parts per million (ppm) downfield of tetramethylsilane. Coupling constants *J* are quoted in Hz. Mass spectra were recorded using EI at 70 eV and high resolution mass spectra were recorded using APCI. For chiral HPLC analyses, a high-pressure binary gradient system equipped with a diode-array detector operating at 254 (220, 280) nm and a 20 μL sample loop was employed. Chiralcel OD-H and Lux Cellulose-1 (250 × 4.6 mm) (5 μm) (cellulose tris-3,5-dimethylphenylcarbamate), Lux Cellulose-2 (250 × 4.6 mm) (5 μm) (cellulose tris-3-chloro-4-methylphenylcarbamate) and Lux Cellulose-4 (250 × 4.6 mm) (5 μm) (cellulose tris-4-chloro-3-methylphenylcarbamate) were used as chiral columns. HPLC-grade hexane and 2-propanol were purchased and used as received. Analyses

were performed in isocratic mode. *n*-Hexane/2-propanol = 9/1 was used as mobile phase, at flow rate 0.8 mL/min and 22 °C. CD spectra were recorded at room temperature using 0.1 mM samples in methanol and a 1 cm quartz cell, with the following conditions: 60 nm/min scanning speed, 1 nm data pitch, 4.0 nm bandwidth, 1 s response time.

3,5-Dibromo-3',5'-diphenyl[4,4']bipyridinyl (2**).** An oven-dried resealable 10-mL tube equipped with a magnetic stir bar was charged with Pd₂(dba)₃ (3.9 mg, 4.24 × 10^{−3} mmol), SPhos (7 mg, 0.017 mmol), bipyridine **1** (100 mg, 0.212 mmol), phenylboronic acid (78 mg, 0.636 mmol), and powdered anhydrous K₃PO₄ (180 mg, 0.848 mmol). The tube was capped, evacuated, and backfilled with argon (with a needle). Dry and degassed toluene (1.5 mL) was added, and the mixture was heated at 100 °C with vigorous stirring for 12 h. The reaction mixture was then allowed to cool to room temperature, concentrated, and purified by column chromatography on silica gel (cyclohexane/ethyl acetate 9/1) to give bipyridine **2** as a white solid (30 mg, 30%): mp 190 °C; ¹H NMR (200 MHz, CDCl₃) δ 7.25 (s, 10H, H_{Ph}), 8.41 (s, 2H), 8.70 (s, 2H); ¹³C NMR (50 MHz, CDCl₃) δ 122.8, 128.1, 128.2, 129.0, 135.6, 136.3, 141.9, 147.2, 149.95, 150.0. MS (ESI) *m/z* 466 (M, 50), 385 (M – Br, 35), 305 (M – Br₂, 100); HRMS calcd for C₂₂H₁₅Br₂N₂ (M + H) 464.9581, found 466.9590.

3,5'-Dibromo-5,3'-diiodo[4,4']bipyridinyl (3**).** Freshly distilled diisopropylamine (1 mL, 6.6 mmol) was added to dry THF (70 mL), and the solution was cooled to −40 °C. A solution of *n*-butyllithium (1.66 M in hexanes, 4 mL, 6.6 mmol) was added dropwise under argon atmosphere. After the solution was stirred for 5 min at −40 °C, 3-bromo-5-iodopyridine (3.4 g, 12 mmol) solubilized in dry THF (50 mL) was added dropwise via a syringe pump (rate: 30 mL/h). The mixture was then stirred at −40 °C for 1 h and cooled to −78 °C, and I₂ (1.68 g, 6.6 mmol) in THF (15 mL) was added dropwise. After the solution was warmed to rt, the reaction was quenched with an aqueous Na₂S₂O₃ and the mixture was extracted with ethyl acetate, dried over MgSO₄ and concentrated. The crude product was purified by chromatography on silica gel to give **3** as a white powder (1.4 g, 41%): mp 180 °C; ¹H NMR (200 MHz, CDCl₃) δ 8.80 (s, 2H), 8.99 (s, 2H); ¹³C NMR (50 MHz, CDCl₃) δ 96.6, 120.2, 151.4, 152.5, 156.2. MS (ESI) *m/z* 566 (M, 80), 439 (M – I, 35), 98 (100); HRMS calcd for C₁₀H₅Br₂I₂N₂ (M + H) 564.6903, found 564.6927.

Typical Procedure for Synthesis of **4.** To a degassed toluene solution (1 mL) containing Pd(PPh₃)₄ (5.8 mg, 0.005 mmol) and bipyridine **3** (56.6 mg, 0.1 mmol) were successively added degassed solutions of arylboronic acid (0.3 mmol, 3 equiv) in methanol (0.5 mL) and Na₂CO₃ (64 mg, 0.6 mmol) in water (0.5 mL). After being heated for 12 h at 100 °C, the reaction mixture was cooled to room temperature, extracted with ethyl acetate, and dried over MgSO₄. After concentration, the residue was purified by chromatography on silica gel to give bipyridine **4**.

3,5'-Dibromo-5,3'-diphenyl[4,4']bipyridinyl (4a**):** mp 188 °C; ¹H NMR (250 MHz, CDCl₃) δ 6.61 (d, *J* = 7.3 Hz, 4H), 7.12 (t, *J* = 7.3 Hz, 4H), 7.23 (t, *J* = 7.3 Hz, 2H), 8.33 (s, 2H), 8.82 (s, 2H); ¹³C NMR (66 MHz, CDCl₃) δ 123.3, 128.0, 128.2, 128.8, 135.3, 137.5, 144.4, 149.2, 150.4; MS (ESI) *m/z* 466 (M, 35), 387 (M – Br, 30), 305 (M – Br₂, 100); HRMS calcd for C₂₂H₁₅Br₂N₂ (M + H) 464.9597, found 464.9587.

3,5'-Dibromo-5,3'-bis(4-methoxyphenyl)[4,4']bipyridinyl (4b**):** mp 167 °C; ¹H NMR (200 MHz, CDCl₃) δ 3.76 (s, 6H), 6.57 (d, *J* = 8.8 Hz, 4H), 6.66 (d, *J* = 8.8 Hz), 8.32 (s, 2H), 8.78 (s, 2H); ¹³C NMR (66 MHz, CDCl₃) δ 55.2, 113.4, 123.2, 127.7, 130.1, 137.3, 144.5, 149.3, 150.0, 159.5; MS (ESI) *m/z* 526 (M, 100), 447 (M – Br, 30), 365 (M – Br₂, 45); HRMS calcd for C₂₄H₁₉Br₂N₂O₂ (M + H) 524.9808, found 524.9796.

3,5'-Dibromo-5,3'-bis(2-methoxyphenyl)[4,4']bipyridinyl (4c**):** mp 190 °C; ¹H NMR (200 MHz, CDCl₃) δ 3.41 (s, 6H), 6.32 (br s, 2H), 6.63 (d, *J* = 7.8 Hz, 2H), 6.65 (dd, *J* = 7.8, 6.8 Hz, 2H), 7.18 (dt, *J* = 7.8, 1.6 Hz, 2H), 8.31 (s, 2H), 8.78 (s, 2H); ¹³C NMR (50 MHz, CDCl₃) δ 54.4, 110.0, 120.1, 123.9, 129.7, 131.4, 145.0, 149.9, 150.9, 156.2; MS (ESI) *m/z* 526 (M, 100), 447 (M – Br, 50), 366 (M – Br₂, 25); HRMS calcd for C₂₄H₁₉Br₂N₂O₂ (M + H) 524.9808, found 524.9800.

3,5'-Dibromo-5,3'-bis(4-chlorophenyl)[4,4']bipyridinyl (4d): mp 248 °C; ^1H NMR (200 MHz, CDCl_3) δ 6.58 (d, J = 8.4 Hz, 4H), 7.14 (d, J = 8.4 Hz, 4H), 8.33 (s, 2H), 8.85 (s, 2H); ^{13}C NMR (50 MHz, CDCl_3) δ 128.4, 130.1, 133.7, 134.8, 136.3, 144.2, 149.1, 149.2, 150.9; MS (ESI) m/z 535 (M, 100), 455 (M - Br, 35), 373 (M - Br₂, 65); HRMS calcd for $\text{C}_{22}\text{H}_{13}\text{Br}_2\text{Cl}_2\text{N}_2$ (M + H) 532.8817, found 532.8825.

3,5'-Dibromo-5,3'-dinaphthalen-1-yl-[4,4']bipyridinyl (4e): mp 202 °C; ^1H NMR (200 MHz, CDCl_3) δ 5.93 (d, J = 8.2 Hz, 2H), 6.43 (ddd, J = 8.2, 7.0, 1.2 Hz, 2H), 6.95 (ddd, J = 8.2, 7.0, 1.0 Hz, 2H), 7.21 (d, J = 2.8 Hz, 2H), 7.25 (d, J = 6.4 Hz, 2H), 7.40 (d, J = 8.2 Hz, 2H), 7.61 (dd, J = 6.4, 2.8 Hz, 2H), 8.27 (s, 2H), 8.89 (s, 2H); ^{13}C NMR (50 MHz, CDCl_3) δ 123.4, 124.3, 125.6, 126.1, 127.3, 127.5, 128.8, 131.3, 132.3, 133.5, 135.4, 145.7, 150.2, 151.5; MS (ESI) m/z 566 (M, 100), 487 (M - Br, 40), 365 (M - Br₂, 90); HRMS calcd for $\text{C}_{30}\text{H}_{19}\text{Br}_2\text{N}_2$ (M + H) 564.9910, found 564.9895.

3,5'-Dibromo-5,3'-bis(4-diphenylaminophenyl)[4,4']bipyridinyl (4f): mp 213 °C; ^1H NMR (200 MHz, CDCl_3) δ 6.52 (d, J = 8.6 Hz, 4H), 6.78 (d, J = 8.6 Hz, 4H), 6.95–7.05 (m, 12 H), 7.10–7.25 (m, 8H), 8.44 (s, 2H), 8.76 (s, 2H); ^{13}C NMR (50 MHz, CDCl_3) δ 121.9, 123.6, 124.8, 128.5, 129.4, 129.6, 144.4, 147.1, 148.0, 149.1, 150.1, 153.8; HRMS calcd for $\text{C}_{46}\text{H}_{33}\text{Br}_2\text{N}_4$ (M + H) 799.1066, found 799.1044.

Typical Procedure for the Synthesis of 5. An oven-dried resealable 10-mL tube equipped with a magnetic stir bar was charged with $\text{PdCl}_2(\text{PPh}_3)_2$ (7 mg, 0.01 mmol), CuI (1.9 mg, 0.01 mmol), and bipyridine 3 (56.6 mg, 0.1 mmol). The tube was capped, evacuated, and backfilled with argon (with a needle). A degassed solution of phenyl- or ferrocenylacetylene (0.3 mmol) in dry triethylamine (1 mL) was added, and the mixture was heated at 70 °C for 12 h. The reaction mixture was then allowed to cool to room temperature, extracted with ethyl acetate, and concentrated. Purification by column chromatography on silica gel (cyclohexane/ethyl acetate 9/1) gave bipyridine 5.

3,5'-Dibromo-5,3'-bis-phenylethynyl[4,4']bipyridinyl (5a): ^1H NMR (250 MHz, CDCl_3) δ 7.15 (dd, J = 7.5, 1.3 Hz, 4H), 7.20–7.40 (m, 6H), 8.83 (s, 2H), 8.84 (s, 2H); ^{13}C NMR (66 MHz, CDCl_3) δ 83.1, 97.4, 120.4, 121.2, 121.6, 128.4, 129.2, 131.6, 147.7, 150.7; MS (ESI) m/z 514 (M, 100), 433 (M - Br, 15), 353 (M - Br₂, 70); HRMS calcd for $\text{C}_{26}\text{H}_{15}\text{Br}_2\text{N}_2$ (M + H) 512.9597, found 512.9622.

3,5'-Dibromo-5,3'-bis-ferrocenylethynyl[4,4']bipyridinyl (5b): mp 210 °C; ^1H NMR (200 MHz, CDCl_3) δ 4.11 (s, 10H, Cp), 4.20 (s, 8H), 8.80 (s, 2H), 8.86 (s, 2H); ^{13}C NMR (50 MHz, CDCl_3) δ 62.9, 69.5, 70.1, 71.5, 71.6, 77.2, 79.7, 98.2, 120.3, 121.9, 147.7, 149.8, 150.2; MS (ESI) m/z 730 (M, 100); HRMS calcd for $\text{C}_{34}\text{H}_{23}\text{Br}_2\text{Fe}_2\text{N}_2$ (M + H) 728.8928, found 728.8948.

Crystal data for 2: $\text{C}_{22}\text{H}_{14}\text{Br}_2\text{N}_2$, M = 466.15, orthorhombic, a = 16.61130(10) Å, b = 12.44370(10) Å, c = 17.7610(2) Å, α = 90.00°, β = 90.00°, γ = 90.00°, V = 3671.31(6) Å³, T = 110(2) K, space group $Pbca$, Z = 8, $\mu(\text{Cu K}\alpha)$ = 5.691 mm⁻¹, 36076 reflections measured, 3854 independent reflections (R_{int} = 0.0302). The final R_i values were 0.0250 ($I > 2\sigma(I)$) and 0.0255 (all data). The final $wR(F^2)$ values were 0.0673 ($I > 2\sigma(I)$) and 0.0676 (all data). The goodness of fit on F^2 was 1.101. CCDC no. CCDC 859199.

Crystal data for 3: $\text{C}_{10}\text{H}_4\text{Br}_2\text{I}_2\text{N}_2$, M = 565.75, triclinic, a = 8.07800(10) Å, b = 11.29930(10) Å, c = 15.5039(2) Å, α = 102.6890(10)°, β = 98.1530(10)°, γ = 90.8930(10)°, V = 1365.01(3) Å³, T = 110(2) K, space group $P1$, Z = 4, $\mu(\text{Mo K}\alpha)$ = 10.437 mm⁻¹, 106245 reflections measured, 27062 independent reflections (R_{int} = 0.0227). Flack parameter = 0.124(5). The final R_i values were 0.0317 ($I > 2\sigma(I)$) and 0.0361 (all data). The final $wR(F^2)$ values were 0.0685 ($I > 2\sigma(I)$) and 0.0707 (all data). The goodness of fit on F^2 was 1.063. CCDC no. CCDC 859200.

Crystal data for 4a: $\text{C}_{22}\text{H}_{14}\text{Br}_2\text{N}_2$, M = 466.17, orthorhombic, a = 7.7417(4) Å, b = 11.2941(6) Å, c = 10.3290(4) Å, α = 90.00°, β = 90.00°, γ = 90.00°, V = 903.12(8) Å³, T = 110(2) K, space group $Pnc2$, Z = 2, $\mu(\text{Mo K}\alpha)$ = 4.530 mm⁻¹, 6477 reflections measured, 2061 independent reflections (R_{int} = 0.0663). Flack parameter = -0.012(17). The final R_i values were 0.0372 ($I > 2\sigma(I)$) and 0.0426 (all data). The final $wR(F^2)$ values were 0.0905 ($I > 2\sigma(I)$) and 0.0945

(all data). The goodness of fit on F^2 was 1.071. CCDC no. CCDC 859201.

Crystal data for 4b: $\text{C}_{24}\text{H}_{18}\text{Br}_2\text{N}_2\text{O}_2$, M = 526.22, monoclinic, a = 8.2955(2) Å, b = 14.6494(3) Å, c = 35.3289(7) Å, α = 90.00°, β = 94.144(2)°, γ = 90.00°, V = 4282.09(16) Å³, T = 110(2) K, space group $P2_1$, Z = 8, $\mu(\text{Mo K}\alpha)$ = 3.832 mm⁻¹, 76167 reflections measured, 19684 independent reflections (R_{int} = 0.0560). Flack parameter = -0.005(5). The final R_i values were 0.0450 ($I > 2\sigma(I)$) and 0.0594 (all data). The final $wR(F^2)$ values were 0.0673 ($I > 2\sigma(I)$) and 0.0711 (all data). The goodness of fit on F^2 was 1.095. CCDC no. CCDC 859202.

Crystal data for 5b: $\text{C}_{34}\text{H}_{22}\text{Br}_2\text{Fe}_2\text{N}_2$, M = 730.06, orthorhombic, a = 11.8083(2) Å, b = 11.9540(2) Å, c = 19.8145(3) Å, α = 90.00°, β = 90.00°, γ = 90.00°, V = 2796.94(8) Å³, T = 110(2) K, space group $P2_12_12_1$, Z = 4, $\mu(\text{Mo K}\alpha)$ = 3.923 mm⁻¹, 40732 reflections measured, 8046 independent reflections (R_{int} = 0.0351). Flack parameter = -0.021(6). The final R_i values were 0.0350 ($I > 2\sigma(I)$) and 0.0435 (all data). The final $wR(F^2)$ values were 0.0639 ($I > 2\sigma(I)$) and 0.0666 (all data). The goodness of fit on F^2 was 1.097. CCDC no. CCDC 859203.

■ ASSOCIATED CONTENT

■ Supporting Information

^1H and ^{13}C spectra of all compounds; X-ray structures of **2**, **4a**, and (*P*)-**5b**; ECD experimental and calculations details; details on calculations of energy barriers of racemization. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

- (1) Birasha, K.; Sarkar, M.; Rajput, L. *Chem. Commun.* **2006**, 4169.
- (2) Monk, P. M. S. *The Viologens: Physicochemical Properties, Synthesis and Applications of the Salts of 4,4'-Bipyridines*; Wiley: Chichester, 2001.
- (3) Paleos, C. M.; Tsiourvas, D. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1696.
- (4) Meiners, C.; Valiyaveetil, S.; Enkelmann, V.; Müllen, K. *J. Mater. Chem.* **1997**, *7*, 2367.
- (5) Ma, L.; Abney, C.; Lin, W. *Chem. Soc. Rev.* **2009**, *38*, 1248.
- (6) Rang, A.; Engeser, M.; Maier, N. M.; Nieger, M.; Lindner, W.; Schalley, C. A. *Chem.—Eur. J.* **2008**, *14*, 3855.
- (7) Sbircea, L.; Sharma, N. D.; Clegg, W.; Harrington, R. W.; Horton, P. N.; Hursthouse, M. B.; Apperley, D. C.; Boyd, D. R.; James, S. L. *Chem. Commun.* **2008**, 5538.
- (8) Jouaiti, A.; Hosseini, M. W.; Kyritsakas, N. *Chem. Commun.* **2002**, 1898.
- (9) Abboud, M.; Mamane, V.; Aubert, E.; Lecomte, C.; Fort, Y. *J. Org. Chem.* **2010**, *75*, 3224.
- (10) Suzuki, A. *Angew. Chem., Int. Ed.* **2011**, *50*, 6722.
- (11) Since $\text{Pd}(\text{PPh}_3)_4$ catalyst was inefficient with bipyridine **2**, the Buchwald method was used: Bardar, T. E.; Walker, S. D.; Martinelli, J. R.; Buchwald, S. L. *J. Am. Chem. Soc.* **2005**, *127*, 4685.
- (12) The phenyl group distribution on the pyridine rings in compounds **2** and **4a** was determined by XRD (see the Supporting Information).

- (13) Sonogashira, K. *J. Organomet. Chem.* **2002**, 653, 46.
- (14) Chromatographic parameters: hexane/2-propanol = 9/1 as mobile phase, flow rate 0.8 mL/min, $T = 22\text{ }^{\circ}\text{C}$. For **3**: Lux Cellulose-2 ($250 \times 4.6\text{ mm}$, $5\text{ }\mu\text{m}$), $\alpha = 1.07$, $R_s = 1.1$; for **4b**: Chiralcel OD-H ($250 \times 4.6\text{ mm}$, $5\text{ }\mu\text{m}$), $\alpha = 1.57$, $R_s = 2.9$.
- (15) Starting from 200 mg of *rac*-**4b** and 20 mg of *rac*-**3**, the HPLC multimilligram recovery led to 60 mg of each atropisomer (*M*)-**4b** and (*P*)-**4b** and to 8 mg and 5 mg of (*M*)-**3** and (*P*)-**3**, respectively. In all cases, to enhance throughput, the technique of overlapping injections was used.
- (16) Frisch et al. See the Supporting Information for the full reference.
- (17) Pipolo, S.; Percudani, R.; Cammi, R. *Org. Biomol. Chem.* **2011**, 9, 5149.
- (18) Kasak, P.; Miklas, R.; Putala, M. *J. Organomet. Chem.* **2001**, 637–639, 318.
- (19) Kasak, P.; Brath, H.; Dubovska, M.; Juricek, M.; Putala, M. *Tetrahedron Lett.* **2004**, 45, 791.
- (20) Krascenicsova, K.; Walla, P.; Kasak, P.; Uray, G.; Kappe, C. O.; Putala, M. *Chem. Commun.* **2004**, 2606.
- (21) Kasak, P.; Putala, M. *Tetrahedron Lett.* **2004**, 45, 5279.
- (22) Juricek, M.; Brath, H.; Kasak, P.; Putala, M. *J. Organomet. Chem.* **2007**, 692, 5279.
- (23) Brath, H.; Meskiva, M.; Putala, M. *Eur. J. Org. Chem.* **2009**, 3315.