DOI: 10.1002/chem.200902562

Resolution of the First Nonracemic Diquats

Jérôme Vachon,[a] Gérald Bernardinelli,[b] and Jérôme Lacour*[a]

Abstract: Three tricyclic diquats with an eight-membered ring were prepared and shown to be the first configurationally stable derivatives of their kind. Resolution was achieved by using chiral hexacoordinated phosphorus BINPHAT and TRISPHAT anions. The diquat cations were obtained in high diastereo- and enantiomeric purity (*ee* > 96% in most cases). X-ray diffraction analysis coupled with circular dichroism (CD) measurements allowed a precise determination of the relative and absolute configuration of the salts. The barriers to racemization of these compounds were calculated by using CD time-course measurements at different temperatures, affording $\Delta G^{\neq}$ values above 25 kcal mol^{-1}. Derivatives **4a**, **4b**, and **4c** are the first eight-membered-ring derivatives with only three ring constraints to be resolved. This manuscript also reports the first procedure to remove TRISPHAT anions after diastereomeric separation.

Keywords: chirality · configuration determination · diquats · racemization barriers · resolution

Introduction

Tricyclic diquats, which are bridged bipyridinium rings linked by a carbocyclic chain, form an important class of positively charged derivatives that have been used for a variety of applications. Diquats are able to accept one electron and form relatively stable radical cations (with a reversible first reduction wave of low potential).[1,2] The resulting unpaired-electron species are known to interfere with photosynthesis and, as such, diquats may display herbicidal activity.[3] Diquats may also be used as structural templates for efficient supramolecular synthesis,[4] as electron acceptors in light-harvesting chromophore-quencher systems,[5] for the construction of ion-pair charge-transfer complexes,[6] and in nonlinear optics.[7]

Diquat derivatives are also noteworthy for their (axial) chirality: the compounds exhibit *P* (or S_a) and *M* (or R_a) atropisomeric conformations owing to the noncoplanarity of the two linked pyridinium rings (Figure 1). The enantiomers are exchangeable owing to rotation about the biaryl axis.

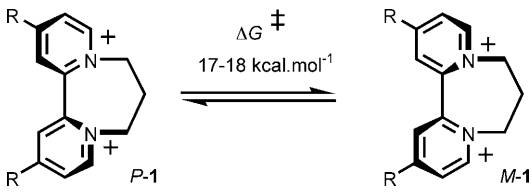


Figure 1. Interconverting conformations *P* (or S_a) and *M* (or R_a) of the tropos seven-membered ring diquats of type **1** (R = H, alkyl).

The dihedral angle adopted between the aromatic moieties depends upon the size of the third nonaromatic cycle (e.g., 51° for the seven-membered ring of **1**),[8] and it was estimated in solution by several spectroscopic methods.[2,9–11]

To the best of our knowledge, stable nonracemic diquats had never been isolated. Diquats had only been reported as configurationally labile molecules or, for the structures that could have been stable (see below), as racemic mixtures of enantiomers. For instance, seven-membered-ring diquats of type **1** are known to interconvert rather rapidly in solution and possess relatively low enantiomerization barriers ($\Delta G^{\neq} \approx 17$–18 kcal mol^{-1}).[9,12] To achieve an imbalance between the interconverting *P* and *M* conformations of **1**, an asymmetric ion pairing with enantiopure anions was considered.[13] Hexacoordinated phosphates BINPHAT **2**[14] and TRISPHAT **3**[15] (Figure 2) were considered to be the best choice in that respect.[16,17] Supramolecular stereocontrol over the configuration of the bipyridinium cations was achieved by the chiral anions acting as noncovalent chiral auxiliaries. A moderate but definite diastereoselectivity was ob-

[a] J. Vachon, Prof. J. Lacour
Organic Chemistry Department, University of Geneva
quai Ernest Ansermet 30, 1211 Genève 4 (Switzerland)
Fax: (+41) 22-379-3215
http://www.unige.ch/sciences/chiorg/lacour/
E-mail: jerome.lacour@unige.ch

[b] Dr. G. Bernardinelli
Laboratory of Crystallography, University of Geneva
quai Ernest Ansermet 24, 1211 Genève 4 (Switzerland)

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/chem.200902562.

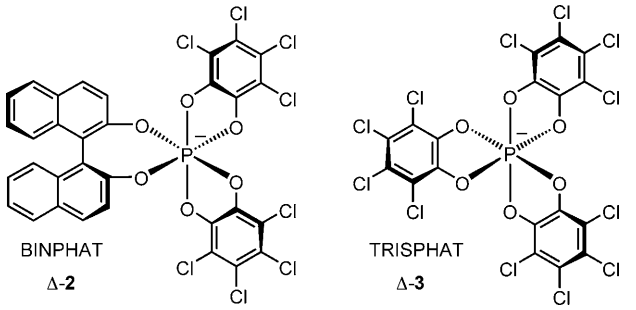


Figure 2. Hexacoordinated phosphorus BINPHAT **2** and TRISPHAT **3** anions (Δ enantiomers).

served ($de < 36\%$, ^{1}H NMR, [D$_6$]acetone (8%) in $CDCl_3$, 298 K).[12]

Nevertheless, as mentioned, nonracemic diquats had never been reported and it was thus debatable whether simple analogues with large enough enantiomerization barriers could be synthesized and subsequently resolved into single enantiomers; the resulting nonracemic dicationic moieties being possible precursors to novel chiral ionic liquids or phase-transfer catalysts.[18] Herein, we report that this is indeed the case because the *P* (S_a) and *M* (R_a) enantiomers of C_2-symmetric diquats **4a** to **4c** were successfully separated. Their configurational stability was ascertained through variable-temperature chiroptical analyses. These molecules are notably the first eight-membered-ring derivatives to be configurationally stable with only three ring constraints.

Results and Discussion

As described above, we looked for alternatives to compounds of type **1** that had a more rigid structure. The search for such atropisomeric (atropos),[19] rather than configurationally flexible (tropos), derivatives was initially pursued on two fronts. The first approach was to compile a complete list of previously reported diquats and then to choose a lead candidate for the target application. In other words, the literature was carefully searched to determine which structures had data indicating a potentially high configurational stability at room temperature. Not counting the recent and elegant examples of helquats,[20] the search rapidly focused on the class of eight-membered-ring bridged diquats of type **4** (Figure 3), which have been previously reported and analyzed.[10] The stereodynamics of salt [**4a**][I]$_2$ (R = H) were studied by variable-temperature ^{1}H NMR spectroscopy in D_2O on a 60 MHz spectrometer. An effective magnetic nonequivalency was observed for the diastereotopic hydrogen atoms ($\Delta\nu = 0.36$ ppm, $J_{AB} = 21.4$ Hz), which did not change upon temperature increase (up to 473 K). This indicated a rather high enantiomerization barrier for **4a** ($\Delta G^{\neq} > 23$ kcal mol^{-1}) by using the formula $\Delta G^{\neq} = R \cdot T_c(22.96 + \ln(T_c/(\Delta\nu^2 J^2)^{1/2}))$ and $T_c = 473$ K. However, an exact value could not be obtained.

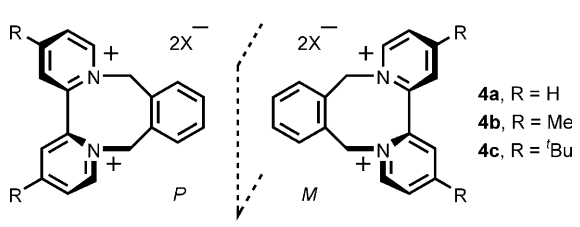


Figure 3. *P* and *M* enantiomers of diquats **4a**, **4b**, and **4c** (R = H, Me, *t*Bu).

The second approach was to analyze a different, yet structurally related family of axially chiral derivatives: the family of *ortho–ortho′*-bridged biphenyl derivatives of types **5** and **6a** (Figure 4). These compounds are the carbocyclic analogues of diquats **1** and **4a**, respectively. They also display atropisomeric conformations, and enantiomerization barriers have been previously reported with values of 11.9 and 20.9 kcal mol^{-1} for **5** and **6a**, respectively.[21] Clearly, the presence of a phenyl-containing eight-membered ring in **6a** has a positive effect on the configurational stability of the biphenyl; the racemization barrier being higher than that of **5** by 9.0 kcal mol^{-1}.

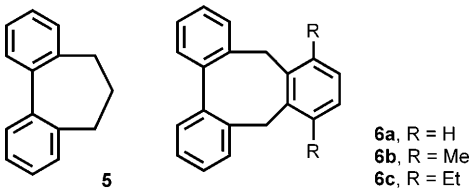
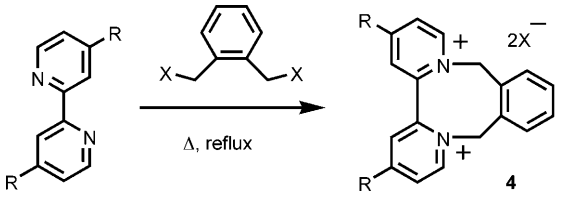


Figure 4. Axially chiral biphenyls **5** and **6**.

Owing to the structural analogies of **6a**/**5** and **4a**/**1**, we presumed that **4** should be rather more configurationally stable that its homologue **1**, with its racemization barrier possibly reaching a value of 25 kcal mol^{-1} or even higher. With this assumption of an atropos nature for compounds **4**, the synthesis and the resolution of derivatives **4a**, **4b**, and **4c** were carried out.

Synthesis of eight-membered-ring diquats: As mentioned, diquat **4a** (R = H) has already been described in the literature.[10] It was synthesized by reacting 2,2′-bipyridine and α,α′-dibrom-*ortho*-xylene (1:1) in acetonitrile at reflux [Eq. (1)]. This exact protocol was used to prepare **4a** and **4b** (R = Me) as their bromide salts (85% and 88%). However, harsher conditions were necessary to synthesize **4c** (R = *t*Bu) from 4,4′-di-*tert*-butyl-2,2′-bipyridine. This re-



(1)

quired 2 equivalents of the more electrophilic α,α′-diiodo-*ortho*-xylene and a higher boiling-point solvent (1,2-dichlorobenzene, 120–160 °C). Salt [**4c**][I]$_2$ was nevertheless isolated by filtration in a reasonable yield (66 %). Once the compounds had been obtained, we quickly verified the previously reported result.[10] A variable-temperature ^{1}H NMR experiment was performed with the more soluble [**4c**][I]$_2$ salt by using a ^{1}H NMR spectrometer with the lowest frequency possible (300 MHz in our case). The results are shown in Figure 5. There are indeed no fluctuations in the NMR signals of the diastereotopic benzylic protons at elevated temperature. After receiving this confirmation of the high conformational stability of **4c**, we studied the resolution of diquats **4a–c**.

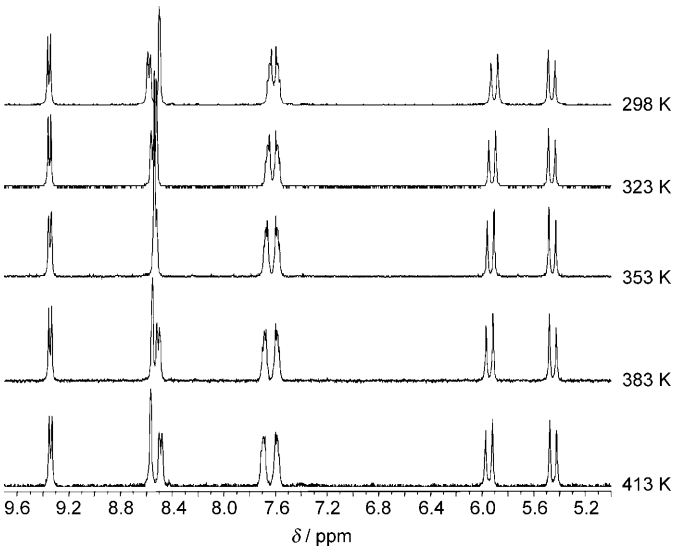


Figure 5. ^{1}H variable-temperature NMR spectra of [**4c**][I]$_2$ (300 MHz, [D$_6$]DMSO, 298–413 K).

Resolution of diquats 4: For the resolution of chiral cations, the most direct and commonly used approach is to form diastereomeric salts by pairing the racemic cations with enantiopure anions and then attempting to separate the diastereomers by using solubility differences.[22] Most protocols utilize enantiopure anions derived from a chiral pool. However, in recent years quite a few examples of successful resolution procedures have been reported by using chiral hexacoordinated phosphorus BINPHAT **2** and TRISPHAT **3** anions as resolving agents.[23,24] These compounds exist as Λ or Δ enantiomers with left- and right-handed propeller geometry (*M* and *P* helicity), respectively. They are, in addition, effective NMR chiral-solvating and asymmetry-inducing reagents.[17] Anion pairing of cations **4a**, **4b**, and **4c** with anions **2** and **3** was, therefore, studied.

Previous studies have shown that these anions often confer to their salts a poor affinity for polar chromatographic phases because they rapidly elute over silica gel/basic alumina.[25] This property was exploited for the preparation of the TRISPHAT salts of cations **4a** to **4c**. Solutions of [*rac*-**4**][X]$_2$ salts (1.0 equiv) in CH_2Cl_2/MeOH (4:1) and of [cinchonidinium][Δ-**3**] (2.1 equiv) in acetone were prepared and mixed together. Preparative column-chromatography experiments (SiO_2, CH_3CN) afforded salts [**4**][Δ-**3**]$_2$ as the only eluted compounds in good chemical yields. However, this protocol was not used to prepare the BINPHAT salts because the products were sensitive to the chromatographic conditions. Methanol solutions of [*rac*-**4**][X]$_2$ (1.0 equiv) and [Me_2NH_2][Δ-**2**] (2.0 equiv) salts were prepared and mixed. Upon ion-exchange metathesis, salts [**4**][Δ-**2**]$_2$ precipitated in decent yields (84–91 %).

NMR spectroscopic analysis of the isolated salts revealed an efficient enantiodifferentiation of chiral cations **4** by the enantiopure counterions. Two sets of signals were observed in both the ^{1}H and the ^{13}C NMR spectra; one set for each of the *P* and *M* enantiomers of compounds **4**. Integration of the respective signals indicated 1:1 to 1.5:1 ratios between the diastereomers in the various salts (see the Experimental Section).

For the separation of the diastereomers, ion-pair chromatographic conditions that have proven effective for the separation of dicationic metal complexes were initially tried.[24,26] However, only one spot was observed in analytical thin-layer chromatography for all the salts by using a variety of solvent or solvent mixtures as the eluent. This indicated concomitant elution of the diastereoisomeric salts and thus a lack of discrimination between the ions during chromatography. Nevertheless, these experiments revealed a global (and surprising) lack of solubility of salts [**4a**][Δ-**2**]$_2$, [**4b**][Δ-**2**]$_2$, [**4c**][Δ-**2**]$_2$, and [**4c**][Δ-**3**]$_2$ in acetonitrile. For example, trituration of salts [**4a**][Δ-**2**]$_2$ and [**4b**][Δ-**2**]$_2$ in CH_3CN led only to an incomplete dissolution of the salts. After filtration, the remaining solids were collected and, upon dissolution in [D$_6$]DMSO and NMR analysis, high levels of diastereomeric purity were observed (diastereomeric ratio, d.r. ≥ 98:2 in both cases, Table 1).

Table 1. Diastereomeric purity of some BINPHAT and TRISPHAT salts upon trituration/precipitation in acetonitrile.

Entry	Salt	Solid/Precipitate (d.r.)[a]	Mother liquor (d.r.)[a]
1	[**4a**][Δ-**2**]$_2$	98:2	35:65
2	[**4b**][Δ-**2**]$_2$	98:2	4:96
3	[**4c**][Δ-**2**]$_2$	94:6	30:70
4	[**4c**][Δ-**3**]$_2$	≥98:2[b]	2.5:97.5[b]

[a] The d.r. measured by ^{1}H NMR spectroscopy (400 MHz, [D$_6$]DMSO (14 %) in $CDCl_3$) unless otherwise stated. [b] The d.r. measured by ^{1}H NMR spectroscopy (400 MHz, CD_3CN (3 %) in $CDCl_3$).

For salts [**4c**][Δ-**2**]$_2$, and [**4c**][Δ-**3**]$_2$, which dissolved completely in CH_3CN at room temperature, it was necessary to cool the resulting (concentrated) solutions to induce precipitation. In the case of [**4c**][Δ-**2**]$_2$, a solid appeared after a few hours at approximately 4 °C, which was filtered. ^{1}H NMR spectroscopic analysis indicated a decent selectivity in the solid fraction (d.r. = 94:6, Table 1, entry 3). For [**4c**][Δ-**3**]$_2$, it

was necessary to lower the temperature to −20 °C. This resulted in the isolation of a solid fraction containing a diastereomerically (and enantiomerically) pure salt (Table 1, entry 4 and Figure 6, spectrum c). The mother liquor contained only traces of this diastereomer; the ^{1}H NMR spectrum displayed almost exclusively the signals of the other diastereomer (Figure 6, spectrum d). All attempts to apply this lower-temperature protocol to salts [**4a**][Δ-**3**]$_2$ and [**4b**][Δ-**3**]$_2$ failed. Regardless, this physical separation of the diastereomeric salts demonstrated that cations **4** are configurationally stable at room temperature.

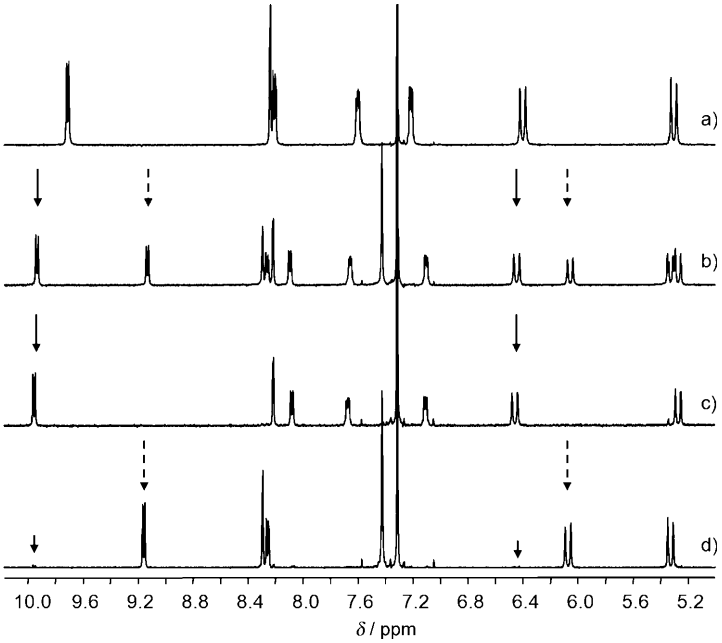


Figure 6. ^{1}H NMR spectra (400 MHz, CD_3CN (3 %) in $CDCl_3$) of a) [**4c**][I]$_2$, b) an approximately 1.2:1 mixture of the diastereomers of [**4c**][Δ-**3**]$_2$, c) the solid fraction (d.r. ≥ 98:2), and d) the mother liquor (d.r. = 2.5:97.5) after precipitation at −20 °C in acetonitrile.

The resolution procedure was then continued by replacing the resolving agents by PF_6 anions. Treatment of the diastereomerically enriched BINPHAT salts with excess HPF_6 in CH_2Cl_2 and addition of Et_2O resulted in the precipitation of the hexafluorophosphate salts with no loss of enantiomeric purity[27] and in excellent yields (94–96 %). The three salts [**4a**][PF_6]$_2$, [**4b**][PF_6]$_2$, and [**4c**][PF_6]$_2$, derived from the solid fractions, were all levorotatory. Those from the mother liquor were, of course, dextrorotatory.

To exchange the TRISPHAT anions, which do not decompose in the presence of a Brönsted acid as anion **2** does, the use of a stronger Lewis acid was required. Excess anhydrous $FeCl_3$ was added to a solution of [*P*-**4c**][Δ-**3**]$_2$ in cold dichloromethane (0 °C) and was stirred for two minutes. The mixture was washed with a saturated aqueous solution of KPF_6 and, after decantation and separation, the organic phase was further filtrated over Celite. Finally, the desired (−)-[*P*-**4c**][PF_6]$_2$ salt was precipitated upon addition of Et_2O to the filtrate. Unfortunately, a moderate but definite racemization of the cation (*ee* = 90 %) was observed during this procedure.

Absolute configuration assignment: After obtaining enantioenriched salts (−)-[**4a**][PF_6]$_2$, (−)-[**4b**][PF_6]$_2$, and (−)-[**4c**][PF_6]$_2$, we turned our attention to determining their absolute configuration. Circular dichroism (CD) experiments were performed in water ($c = 1\times10^{-5}$ or 3×10^{-5} M), and essentially congruent spectra were obtained (Figure 7). This result demonstrated without ambiguity that the configuration of the predominant enantiomer is the same in all three levorotary salts.

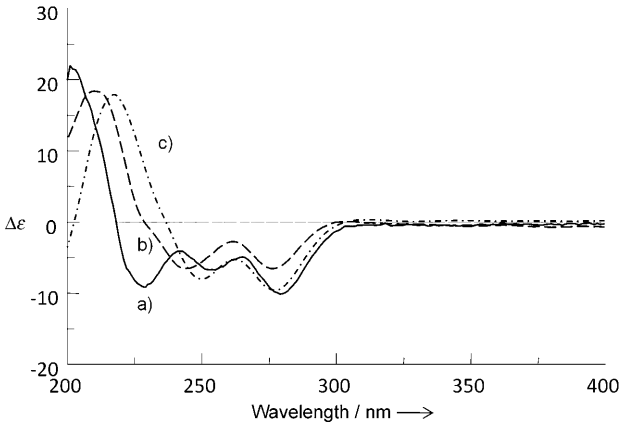


Figure 7. CD spectra in water of a) (−)-[**4a**][PF_6]$_2$ ($c = 1\cdot10^{-5}$ M, ——), b) (−)-[**4b**][PF_6]$_2$ ($c = 1\cdot10^{-5}$ M, -----) and c) (−)-[**4c**][PF_6]$_2$ ($c = 1\cdot10^{-5}$ M, –•–•).

The three spectra exhibited negative Cotton effects around 250 and 275 nm. Although it was tempting to assign a *P* (or S_a) configuration to these axially chiral dications based on the CD guidelines established by Mislow and Sandström for the absolute configuration assignment of biphenyls,[28] the structural analogy between diquats **4a**, **4b**, **4c**, and simple biphenyls was not deemed to be sufficient, and care was taken to assign the absolute configuration by another method.

From the precipitate fraction of [**4c**][Δ-**3**]$_2$, precursor to salt (−)-[**4c**][PF_6]$_2$, monocrystals were obtained by slow diffusion of hexane in acetone, and an X-ray structural analysis was performed. The results established the presence of a single diastereomeric species within the solid (Figure 8). The value obtained for the Flack parameter ($x = -0.02(6)$) confirmed the Δ configuration for the TRISPHAT anions and established an unambiguous *P* (S_a) configuration for **4c** by using this internal reference. Considering that the *P* configuration of **4c** remains unchanged upon the removal of the hexacoordinated phosphate anions **3**, then (−)-[**4c**][PF_6]$_2$ and all the other levorotatory salts present diquat cations of *P* configuration.

Compound **4c** exhibits a rather large dihedral angle θ of 62° around the central bond joining the pyridinium rings

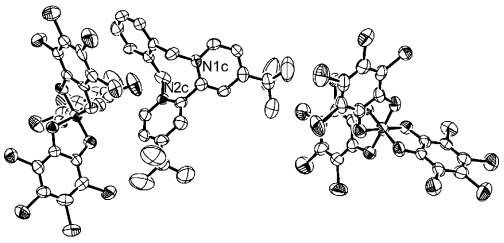


Figure 8. X-ray diffraction analysis of [*P*-**4c**][Δ-**3**]$_2$ (precipitate fraction). Five acetone molecules and all hydrogen atoms are omitted.

(Figure 8). This is in agreement with that measured for three aliphatic eight-membered-ring diquats ($61° < \theta < 70°$), the structures of which can be found in the Cambridge Structural Database. These moieties are shown in Figure 9;

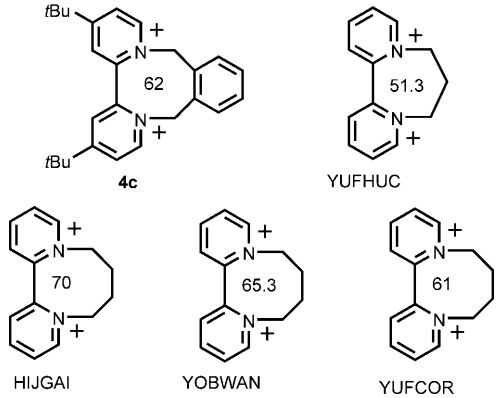


Figure 9. Eight- and seven-membered diquats and dihedral angles at the biaryl junction.

the CSD reference codes (HIJGAI,[29] YOBWAN,[30] YUFCOR[31]) corresponding to the structures and the dihedral angles are given on the drawing. The only seven-membered ring found (YUFHUC)[8] exhibits a much reduced value of 51.3°.

Configurational stability: Before carrying out the above experiments, we could only infer that compounds of type **4** would be configurationally stable. Precise values for the racemization barriers were unknown. To correct this situation, enantioenriched samples of [**4a**][PF$_6$]$_2$, [**4b**][PF$_6$]$_2$, and [**4c**][PF$_6$]$_2$ were heated in water at four different temperatures and the racemization of the samples was monitored by using CD spectroscopy. The results of a typical experiment are shown in Figure 10. A decrease of all absorptions was observed on heating an enantioenriched sample of (+)-[*M*-**4c**][PF$_6$]$_2$ at 60 °C. After a certain period (≈50 min in this case), the value reaches zero, which indicates complete racemization. For **4c**, samples were heated at 50, 60, 70, and 80 °C. For compounds **4a** and **4b**, a slightly higher range of temperature (70–95 °C) was necessary in order to obtain decent racemization kinetics.

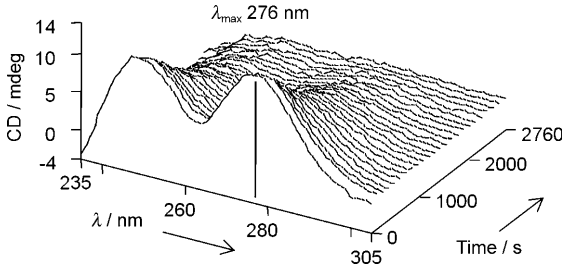


Figure 10. CD time-course measurements ($\lambda = 235$–305 nm) of salt (+)-[(*M*)-**4c**][PF$_6$]$_2$ in water (60 °C, c 10^{-5} M).

In these experiments, it was actually easier to monitor a single wavelength (276 nm, Figure 11) and to use dextrorotatory samples presenting positive Cotton effects at lower

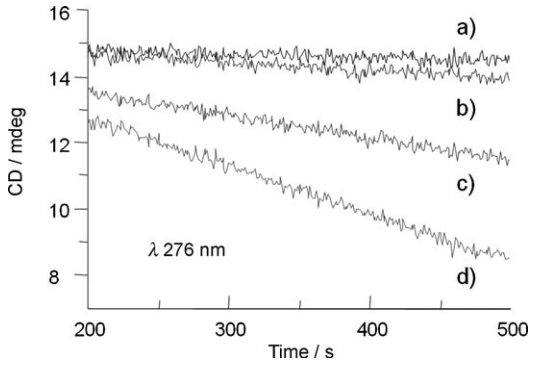


Figure 11. CD time-course measurements ($\lambda = 276$ nm) at a) 50, b) 60, c) 70, and d) 80 °C of salt (+)-[(*M*)-**4c**][PF$_6$]$_2$ in water ($c = 10^{-5}$ M).

energy. Kinetic constants were calculated at the four analyzed temperatures, and the determination of all activation parameters were realized for each cation (E_a, A, $\Delta H^{\neq}$, $\Delta S^{\neq}$, and $\Delta G^{\neq}$, see the Supporting Information). The results are reported in Table 2. The values for the free energy of activation are in accordance with our expectations (≈25 kcal mol^{-1} and higher); [**4c**][PF$_6$]$_2$ (Table 2, entry 3) exhibited the smallest value. These values correspond to half-lives of 13, 127, and 9.5 days at 20 °C for salts [**4a**][PF$_6$]$_2$, [**4b**][PF$_6$]$_2$, and [**4c**][PF$_6$]$_2$, respectively. The entropy values are rather low, which is expected for an intramolecular racemization process.

Interestingly, the substituents on the core structure have only a moderate influence on the racemization barrier. Just

Table 2. Racemization of diquats **4a**, **4b**, and **4c**: activation parameters.

Entry	Salt	E_a[a]	A [s^{-1}]	$\Delta H^{\neq}$[a]	$\Delta S^{\neq}$[b]	$\Delta G^{\neq}$[a,c]
1	[**4a**][PF$_6$]$_2$	25.4	5.8×10^{12}	24.8	−2.1	25.5
2	[**4b**][PF$_6$]$_2$	29.0	2.6×10^{14}	28.4	5.4	26.8
3	[**4c**][PF$_6$]$_2$	24.8	2.7×10^{12}	24.2	−3.6	25.3

[a] In kcal mol^{-1}; precision ±0.2. [b] In cal J^{-1} mol^{-1} [c] At 20 °C.

a 1.4 kcal mol^{-1} difference is observed between the lowest (R = *t*Bu) and highest (R = Me) $\Delta G^{\neq}$ value. Previously, a larger difference was observed in the study of compounds **6a**, **6b**, and **6c** by Rabinovitz and co-workers ($\Delta G^{\neq}$ = 20.1, 17.3, and 17.6 kcal mol^{-1}, respectively).[21] In both series, the derivatives that present the lowest barriers are those carrying the largest residues. Probably, the bulky substituents on these derivatives **4c** and **6c** raise the energy of the ground states more effectively than that of the transition states. This observation can probably be correlated with the (difficult) synthesis of **4c** that requires a better electrophile and more elevated temperatures.

Conclusion

In conclusion, as in numerous bridged biphenyls, the free energy of activation for racemization was found to depend on the degree by which the bridge restricts freedom of rotation about the biaryl axis because compounds **4a**, **4b**, and **4c** were shown to be the first configurationally stable diquats. The degree of restriction is determined by the structure of the bridge and moderately by the functional groups present on the biaryl component. Notably, derivatives **4a**, **4b**, and **4c** are the first compounds with an eight-membered ring and with only three ring constraints to be resolved. This manuscript also reports the first procedure to remove TRISPHAT anions after diastereomeric separation.

Experimental Section

All reactions were carried out under dry N_2 or Ar by means of an inert gas/vacuum double-manifold line with magnetic stirring unless otherwise stated. Solvents were dried and distilled prior to use: toluene was freshly distilled from sodium, dichloromethane and hexane were freshly distilled from calcium hydride, and diethyl ether and tetrahydrofuran were freshly distilled from sodium benzophenone. $CHCl_3$, CH_2Cl_2, $CDCl_3$, and CD_2Cl_2 (SDS) were filtered on basic alumina. Analytical thin-layer chromatography (TLC) was performed with Merck SIL G/UV$_{254}$ plates or Flucka 0.25 mm basic alumina (pH 9.9) plates. Visualization of the developed chromatogram was performed by UV/Vis detection. Organic solutions were concentrated under reduced pressure on a Büchi rotary evaporator. Unless otherwise stated, column chromatography (silica gel 60, 40 μm, or Fluka basic alumina type 5016 A) was performed in air and under pressure (0.1–0.3 bar).

NMR spectra were recorded on a Bruker AMX-400 at room temperature unless otherwise stated. ^{1}H NMR spectra: chemical shifts are given in ppm relative to Me_4Si with the solvent resonance used as the internal standard. ^{31}P NMR (162 MHz) spectra: chemical shifts are reported in ppm relative to H_3PO_4. ^{13}C NMR (100 MHz) spectra: chemical shifts are given in ppm relative to Me_4Si, with the solvent resonance used as the internal standard (δ = 77.0 ($CDCl_3$), 39.5 ([D$_6$]DMSO), 53.8 ppm (CD_2Cl_2)). Assignments were achieved by using COSY, HETCOR, and/or NOESY experiments. IR spectra were recorded with a Perkin–Elmer 1650 FTIR spectrometer using diamond ATR Golden Gate sampling. Melting points (m.p.) were measured in open capillary tubes on a Stuart Scientific SMP3 melting-point apparatus and are uncorrected. Electrospray mass spectra (ESMS) were obtained on a Finnigan SSQ 7000 spectrometer, and EIMS spectra were obtained on a Varian CH4 or SM1 spectrometer by using an ionizing voltage 70 eV by the Department of Mass Spectroscopy at the University of Geneva. UV/Vis spectra were recorded on a CARY-1E spectrometer in a 1.0 cm quartz cell; λ_{max} are given in nm and the molar adsorption coefficient ε in cm^{-1} dm^3 mol^{-1}. Circular dichroism spectra were recorded on a JASCO J-715 polarimeter in a 1.0 cm quartz cell; λ are given in nm and molar circular dichroic absorptions ($\Delta\varepsilon$) in cm^2 mmol^{-1}). Optical rotations were measured on a Perkin–Elmer 241 polarimeter in a thermostated (20 °C) 10.0 cm long microcell with high-pressure lamps of sodium or mercury and are reported as follows: $[\alpha]_\lambda^{20}$ (*c* (g per 100 mL), solvent). X-ray diffraction structures were solved at the "Laboratoire de Cristallographie aux rayons X, Service de Resolution Structurale par Diffraction des Rayons X" by Dr. G. Bernardinelli.

Diquat 4a

*[**4a**][Br]$_2$*: A sealed tube containing 2,2′-dipyridyl (107 mg, 0.685 mmol) and α,α′-dibromo-*ortho*-xylene (181 mg, 0.685 eq) in acetonitrile (2.5 mL) was heated at 90 °C for 15 h. After cooling, Et_2O (5 mL) was added, and the resulting precipitate was filtered and washed with Et_2O to obtain the desired compound as a white solid (yield = 200 mg, 70 %). M.p. 298 °C; ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 9.53 (d, 2H, *J* = 5.6 Hz), 8.97 (td, 2H, *J* = 1.0 Hz and 7.8 Hz), 8.55 (td, 2H, *J* = 1.3 Hz and 7.3 Hz), 8.51 (dd, 2H, *J* = 1.0 Hz and 7.8 Hz), 7.69 (m, 2H), 7.58 (m, 2H), 6.00 (d, 2H, *J* = 15.8 Hz), 5.48 ppm (d, 2H, *J* = 15.8 Hz); ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 148.3 (CH), 147.6 (CH), 144.7 (C^{IV}), 131.6 (CH and C^{IV}), 131.0 (CH), 130.5 (CH), 130.0 (CH), 60.2 ppm (CH_2); IR (neat): $\tilde{\nu}$ = 3007, 2985, 1622, 1585, 1505, 1470, 1193, 1164 cm^{-1}; UV/Vis (CH_3CN, 10^{-5} M): λ_{max} (ε) = 201 (3.53×10^5), 278 nm (1.15×10^5); MS (ES$^+$): *m*/*z* (%): 180.1 (100) [*M*−C_8H_8+1], 259.3 (50) [*M*−1].

Ion metathesis with Δ-BINPHAT: A solution of [**4a**][Br]$_2$ (55.0 mg, 0.131 mmol) in methanol (3 mL) was added to a solution of [Me_2NH_2][Δ-**2**] (223.6 mg, 0.262 mmol) in methanol (10 mL). The mixture was stirred for about 5 min. The resulting precipitate was filtered and washed with Et_2O. The diastereomeric salt was obtained as a yellow solid (yield = 210 mg, 86 %), containing 60 % of [*P*-**4a**][Δ-**2**]$_2$ and 40 % of [*M*-**4a**][Δ-**2**]$_2$ (^{1}H NMR analysis in a mixture of [D$_6$]DMSO (14 %) in $CDCl_3$).

Separation of the diastereomers: Acetonitrile (10 mL) was added to a round-bottom flask containing the mixture of diastereomers [**4a**][Δ-**2**]$_2$ (180 mg). The solid was triturated until a thin powder was obtained. The yellow precipitate was filtered to afford [*P*-**4a**][Δ-**2**]$_2$ (yield = 91 mg, ≈50 %, d.r. = 98:2) as a yellow solid. After evaporation to dryness of the mother liquor, [*M*-**4a**][Δ-**2**]$_2$ was obtained as a yellow solid (yield = 77 mg, ≈43 %, d.r. = 65:35).

*Analysis for [P-**4a**][Δ-2]$_2$*: Yellow solid; d.r. = 98:2; m.p. 235 °C; $[\alpha]_D^{20}$ = −43.4 (*c* = 0.1, CH_3CN); ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 9.44 (s, 2H), 8.94 (s, 2H), 8.52 (b, 4H), 7.96 (d, 4H, *J* = 8.1 Hz, 2), 7.84 (d, 4H, *J* = 8.6 Hz, 2), 7.62 (s, 2H), 7.57 (s, 2H), 7.40 (m, 4H, 2), 7.27 (d, 4H, *J* = 3.3 Hz, 2), 6.57 (d, 8H, *J* = 8.8 Hz, 2), 5.90 (d, 2H, *J* = 13.4 Hz), 5.48 ppm (d, 2H, *J* = 14.7 Hz); ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 151.8 (C^{IV}, d, *J* = 12.4 Hz, 2), 148.4 (CH), 147.6 (CH), 144.7 (C^{IV}), 142.6 (C^{IV}, d, *J* = 5.8 Hz, 2), 142.1 (C^{IV}, d, *J* = 9.1 Hz, 2), 131.8 (C^{IV}), 131.6 (CH), 131.5(C^{IV}, 2), 131.0 (CH), 130.5 (CH), 130.0 (CH cation and C^{IV}, 2), 129.1 (CH, 2), 128.3 (CH, 2), 126.3 (CH, 2), 125.7 (CH, 2), 124.1 (CH, 2), 122.6 (CH, d, *J* = 3.3 Hz, 2), 122.3 (C^{IV}, d, *J* = 3.3 Hz, 2), 121.4 (C^{IV}, 2), 119.9 (C^{IV}, 2), 112.9 (C^{IV}, d, *J* = 15.7 Hz, 2), 112.7 (C^{IV}, d, *J* = 14.1 Hz, 2), 60.2 ppm (CH_2); ^{31}P NMR (162 MHz, [D$_6$]DMSO): δ = −83.99 ppm; IR (neat): $\tilde{\nu}$ = 3077, 1614, 1592, 1450, 1235, 947, 819 cm^{-1}; UV/Vis (CH_3CN, 10^{-5} M): λ_{max} (ε) = 220 (2.81×10^5), 302 (2.9×10^4), 329 nm (1.5×10^4); CD (CH_3CN, 10^{-5} M): λ ($\Delta\varepsilon$) = 207 (−151.4), 231 (333.8), 244 (−120.7), 264 (38.7), 298 (−6.9), 328 cm^2 mmol^{-1} (−2.5); MS (ES$^-$): *m*/*z* (%): 807.0 (100) [**2**]; MS (ES$^+$): *m*/*z* (%): 184.4 (50), 259.4 (50), [*M*−1], 371.5 (100).

General procedure for the ion exchange of BINPHAT anions to PF_6: Aqueous HPF_6 (≈7.9 M, 10 equiv) was added to a suspension of [**4a**][Δ-**2**]$_2$, [**4b**][Δ-**2**]$_2$, or [**4a**][Δ-**2**]$_2$ in CH_2Cl_2 (≈1 mL per 0.01 mmol of substrate). After stirring for 2 min, Et_2O was added to precipitate the desired [**4a**][PF_6]$_2$, [**4b**][PF_6]$_2$, or [**4c**][PF_6]$_2$ salt, which was thoroughly washed with Et_2O and pentane.

*[P-**4a**][PF_6]$_2$*: White solid; *ee* = 96 %; yield 96 %; m.p. 267 °C; $[\alpha]_D^{20}$ = −207 (*c* = 0.1, H_2O); IR (neat): $\tilde{\nu}$ = 3090, 1622, 1585, 1501, 1469, 1311, 1197, 1164, 832 cm^{-1}; ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 9.47 (d, 2H, *J* = 5.6 Hz), 8.96 (t, 2H, *J* = 7.8 Hz), 8.54 (t, 2H, *J* = 6.7 Hz), 8.48 (d, 2H,

$J=7.8$ Hz), 7.65 (m, 2H), 7.59 (m, 2H), 5.92 (d, 2H, $J=15.8$ Hz), 5.49 ppm (d, 2H, $J=15.8$ Hz); ^{13}C NMR (100 MHz, [D$_6$]DMSO): $\delta=$ 148.4 (CH), 147.6 (CH), 144.7 (C^{IV}), 131.6 (CH), 131.5 (C^{IV}), 131.0 (CH), 130.4 (CH), 130.0 (CH), 61.4 ppm (CH$_2$); UV/Vis (H$_2$O, 10^{-5} M): λ_{max} (ε) = 200 (3.1×10^4), 239 (3×10^3), 278 nm (8×10^3); CD (H$_2$O, 10^{-5} M): λ ($\Delta\varepsilon$) = 203 (24.7), 229 (−9.9), 242 (−4.1), 253 (−7.1), 266 (−5.11), 279 cm^{2}mmol^{-1} (−10.97); MS (ES$^+$): *m*/*z* (%): 182.1 (100), 259.4 (50), [*M*−1].

(+)-[*M*-4a][PF$_6$]$_2$: The compound was instead obtained by resolution with a Λ-BINPHAT salt. *ee* = 96%; $[\alpha]_D^{20}$ +201 (*c* = 0.1, H$_2$O).

Diquat 4b

[4b][Br]$_2$: A sealed tube containing 4,4′-dimethyl-2,2′-dipyridyl (117 mg, 0.636 mmol) and α,α′-dibromo-*ortho*-xylene (168 mg, 0.636 mmol) in acetonitrile (2.5 mL) was heated at 90 °C for 15 h. After cooling, Et$_2$O (5 mL) was added. The resulting precipitate was filtered and washed with Et$_2$O to obtain the desired compound as a pale-yellow solid (yield = 250 mg, 88%). M.p. 293 °C; ^{1}H NMR (400 MHz, [D$_6$]DMSO): $\delta=9.36$ (d, 2H, $J=6.8$ Hz), 8.37 (m, 4H), 7.66 (m, 2H), 7.56 (m, 2H), 5.92 (d, 2H, $J=15.9$ Hz), 5.46 (d, 2H, $J=15.9$ Hz), 2.74 ppm (s, 6H); ^{13}C NMR (100 MHz, [D$_6$]DMSO): $\delta=161.1$ (C^{IV}), 147.1 (CH), 143.4 (C^{IV}), 131.6 (C^{IV}), 131.4 (CH), 130.9 (CH), 130.7 (CH), 129.9 (CH), 60.4 (CH$_2$), 21.8 ppm (CH$_3$); IR (neat): $\tilde{\nu}=$3439, 2984, 2928, 1623, 1447, 1164, 845 cm^{-1}; UV/Vis (CH$_3$CN, 10^{-5} M): λ_{max} (log ε): 215 (1.51), 230 (1.16), 274 (0.82); MS (ES$^+$): *m*/*z* (%): 184.6 (95) [*M*−C$_8$H$_8$+1], 287.6 (100) [*M*−1].

Ion metathesis with Δ-BINPHAT: A solution of [**4b**][Br]$_2$ (55.0 mg, 0.135 mmol) in methanol (2 mL) was added to a solution of [Me$_2$NH$_2$][Δ-**2**] (230.5 mg, 0.270 mmol) in methanol (10 mL). The mixture was stirred for about 5 min. The resulting precipitate was filtered and washed with Et$_2$O. The diastereomeric salt was obtained as a yellow solid (yield = 216 mg, 84%) containing 56% of [*P*-**4b**][Δ-**2**]$_2$ and 44% of [*M*-**4b**][Δ-**2**]$_2$. ^{1}H NMR analysis was carried out in a mixture of [D$_6$]DMSO (14%) in CDCl$_3$.

Separation of the diastereomers: Acetonitrile (10 mL) was added to a round-bottom flask containing [**4b**][Δ-**2**]$_2$ (194 mg). The solid was triturated until a thin powder was obtained. The yellow precipitate was filtered to afford [*P*-**4b**][Δ-**2**]$_2$ (yield = 107 mg, ≈55%, d.r. = 98:2) as a yellow solid. After evaporation to dryness of the mother liquor, [*M*-**4b**]-[Δ-**2**]$_2$ was obtained as a yellow solid (yield = 78 mg, ≈40%, d.r. = 96:4).

[P-4b][Δ-2]$_2$: Yellow solid; d.r. = 98:2; m.p. 255 °C; $[\alpha]_D^{20}=-24.5$ (*c* = 0.04, CH$_3$CN); ^{1}H NMR (400 MHz, [D$_6$]DMSO): $\delta=9.26$ (d, 2H, $J=$ 5.3 Hz), 8.32 (b, 4H), 7.96 (d, 4H, $J=8.1$ Hz, 2), 7.84 (d, 4H, $J=8.8$ Hz, 2), 7.57 (m, 4H), 7.40 (m, 4H, 2), 7.28 (m, 8H, 2), 6.59 (d, 4H, $J=8.8$ Hz, 2), 5.80 (d, 2H, $J=16.1$ Hz), 5.44 (d, 2H, $J=15.6$ Hz), 2.71 ppm (s, 6H); ^{13}C NMR (100 MHz, [D$_6$]DMSO): $\delta=161.1$ (C^{IV}), 151.8 (C^{IV}, d, $J=$ 12.4 Hz, 2), 147.1 (CH), 143.8 (C^{IV}), 142.6 (C^{IV}, d, $J=5.0$ Hz, 2), 142.1 (C^{IV}, d, $J=9.1$ Hz, 2), 131.8 (C^{IV}), 131.5 (C^{IV}, 2), 131.4 (CH), 130.9 (CH), 130.6 (CH), 130.0 (C^{IV}, 2), 129.9 (CH), 129.1 (CH, 2), 128.3 (CH, 2), 126.3 (CH, 2), 125.7 (CH, 2), 124.1 (CH, 2), 122.6 (CH, d, $J=4.1$ Hz, 2), 122.3 (C^{IV}, d, $J=3.3$ Hz, 2), 121.4 (C^{IV}, 2), 119.9 (C^{IV}, 2), 112.9 (C^{IV}, d, $J=$ 15.7 Hz, 2), 112.7 (C^{IV}, d, $J=15.0$ Hz, 2), 60.5 (CH$_2$), 21.8 ppm (CH$_3$); ^{31}P NMR (162 MHz, [D$_6$]DMSO): $\delta=-83.83$ ppm; IR (neat): $\tilde{\nu}=$2971, 1623, 1445, 1389, 1236, 989, 817 cm^{-1}; UV/Vis (CH$_3$CN, 10^{-5} M): λ_{max} (ε) = 220 (3.42×10^5), 274 (2.17×10^5), 323 nm (1.9×10^4); CD (CH$_3$CN, 10^{-5} M): λ ($\Delta\varepsilon$) = 207 (−178.3), 231 (396.8), 244 (−150.3), 264 (50.7), 298 (−10.7), 328 cm^{2}mmol^{-1} (−3.4); MS (ES$^-$): *m*/*z* (%): 807.0 (100), BINPHAT; MS (ES$^+$): *m*/*z* (%): 184.1 (80), [*M*−C$_8$H$_8$+1], 371.5 (100).

[M-4b][Δ-2]$_2$: Yellow solid; d.r. = 96:4; m.p. 250 °C; $[\alpha]_D^{20}=28.4$ (*c* = 0.1, CH$_3$CN); ^{1}H NMR (400 MHz, [D$_6$]DMSO): $\delta=9.27$ (b, 2H), 8.32 (b, 4H), 7.95 (d, 4H, $J=6.8$ Hz, 2), 7.83 (d, 4H, $J=7.3$ Hz, 2), 7.57 (d, 4H, $J=12.3$ Hz), 7.40 (b, 4H, 2), 7.27 (b, 8H, 2), 6.57 (d, 4H, $J=8.1$ Hz, 2), 5.83 (d, 2H, $J=15.9$ Hz), 5.43 (d, 2H, $J=15.6$ Hz), 2.71 ppm (s, 6H); ^{13}C NMR (100 MHz, [D$_6$]DMSO): $\delta=161.6$ (C^{IV}), 152.3 (C^{IV}, d, $J=$ 12.2 Hz, 2), 147.6 (CH), 144.3 (C^{IV}), 143.0 (C^{IV}, d, $J=5.8$ Hz, 2), 142.6 (C^{IV}, d, $J=9.0$ Hz, 2), 132.3 (C^{IV}), 132.0 (C^{IV}, 2), 131.9 (CH), 131.4 (CH), 131.1 (CH), 130.5 (C^{IV}, 2), 130.4 (CH), 129.6 (CH, 2), 128.8 (CH, 2), 126.8 (C^{IV}), 126.3 (CH, 2), 126.1 (CH, 2), 124.9 (CH, 2), 123.0 (CH, d, $J=$ 3.2 Hz, 2), 122.8 (C^{IV}, d, $J=3.2$ Hz, 2), 121.8 (C^{IV}, 2), 120.4 (C^{IV}, 2), 113.4 (C^{IV}, d, $J=11.6$ Hz, 2), 113.1 (C^{IV}, d, $J=10.3$ Hz, 2), 60.9 (CH$_2$), 22.3 ppm (CH$_3$); ^{31}P NMR (162 MHz, [D$_6$]DMSO): $\delta=-84.01$ ppm; IR (neat): $\tilde{\nu}=$ 3049, 2971, 1624, 1591, 1449, 1388, 1235, 991, 817 cm^{-1}; UV/Vis (CH$_3$CN, 10^{-5} M): λ_{max} (ε) = 222 (3.78×10^5), 301 (7.0×10^4), 329 nm (3.3×10^4); CD (CH$_3$CN, 10^{-5} M): λ ($\Delta\varepsilon$) = 245 (−88.5), 264 (29.2), 302 (−14.1), 330 cm^{2}mmol^{-1} (−8.5); MS (ES$^-$): *m*/*z* (%): 807.0 (100) BINPHAT; MS (ES$^+$): *m*/*z* (%): 184.1 (80) [*M*−C$_8$H$_8$+1], 371.5 (100).

[P-4b][PF$_6$]$_2$: The compound was obtained as a white solid (96%, *ee* = 96%) by using the general procedure of exchange of anions **2** to PF$_6$. M.p. 270 °C; $[\alpha]_D^{20}=-183$ (*c* = 0.1, H$_2$O); IR (neat): $\tilde{\nu}=$3119, 1633, 1588, 1515, 1455, 1172, 824 cm^{-1}; ^{1}H NMR (400 MHz, [D$_6$]DMSO): $\delta=9.28$ (d, 2H, $J=6.3$ Hz), 8.35 (m, 4H), 7.62 (m, 2H), 7.57 (m, 2H), 5.82 (d, 2H, $J=15.9$ Hz), 5.45 (d, 2H, $J=15.9$ Hz), 2.74 ppm (s, 6H); ^{13}C NMR (100 MHz, [D$_6$]DMSO): $\delta=161.2$ (C^{IV}), 147.1 (CH), 143.8 (C^{IV}), 131.6 (C^{IV}), 131.5 (CH), 130.9 (CH), 130.6 (CH), 129.9 (CH), 60.5 (CH$_2$), 21.8 ppm (CH$_3$); UV/Vis (CH$_3$CN, 10^{-5} M): λ_{max} (ε) = 206 (2.0×10^4), 231 (9×10^3), 274 nm (7×10^3); MS (ES$^+$): *m*/*z* (%): 184.6 (90), [*M*−C$_8$H$_8$+1], 287.6 (100) [*M*−1].

(+)-[M-4b][PF$_6$]$_2$: The compound was obtained from mother liquors of the resolution with Δ-**2**. *ee* = 92%; $[\alpha]_D^{20}=+145$ (*c* = 0.1 in H$_2$O).

Diquat 4c

[4c][I]$_2$: A sealed tube containing 4,4′-di-*tert*-butyl-2,2′-dipyridyl (305.5 mg, 0.220 mmol), α,α′-diiodo-*ortho*-xylene (815 mg, 0.439 mmol), and 1,2 dichlorobenzene (freshly distilled on CaH$_2$) was heated from 120 °C to 160 °C over a period of 4 h. After cooling, the yellow precipitate was filtered then thoroughly washed with pentane to afford [**4c**][I]$_2$ as a yellow powder (yield = 460 mg, 65%). M.p. 258 °C; ^{1}H NMR (400 MHz, CD$_3$CN): $\delta=9.39$ (d, 2H, $J=6.5$ Hz), 8.63 (d, 2H, $J=2.0$ Hz), 8.41 (dd, 2H, $J=2.3$ Hz and 6.6 Hz), 7.81 (dd, 2H, $J=3.5$ Hz and 5.3 Hz), 7.59 (dd, 2H, $J=3.4$ Hz and 5.7 Hz), 6.10 (d, 2H, $J=16.2$ Hz), 5.34 (d, 2H, $J=16.2$ Hz), 1.52 ppm (s, 18H); ^{13}C NMR (100 MHz, CD$_3$CN): $\delta=173.6$ (C^{IV}), 147.1 (CH), 144.4 (C^{IV}), 131.1 (CH), 130.4 (CH), 128.7 (CH), 128.6 (CH), 60.95 (CH$_2$), 37.3 (C^{IV}), 29.1 ppm (CH$_3$); IR (neat): $\tilde{\nu}=$3420, 3038, 2959, 1621, 1452, 1116, 847 cm^{-1}; UV/Vis (CH$_3$CN, 10^{-5} M): λ_{max} (ε) = 207 (7.3×10^4), 248 (6.3×10^4), 290 nm (4.2×10^4); MS (ES$^+$): *m*/*z* (%): 186.6 (1) [*M*/2], 403.5 (100).

Ion metathesis with Δ-BINPHAT: A solution of [Me$_2$NH$_2$][Δ-**2**] (340.5 mg, 0.399 mmol) in acetone (10 mL) was added to a solution of [**4c**][I]$_2$ (100 mg, 0.159 mmol) in a 5:1 mixture of CH$_2$Cl$_2$/MeOH (3 mL). After 5 min of stirring, the solution was evaporated to dryness. After filtration on basic alumina (eluent acetonitrile), an orange solid was obtained containing an almost 1:1 mixture (found from ^{1}H NMR spectroscopic analysis in a mixture of [D$_6$]DMSO (14%) in CDCl$_3$) of the two diastereomers (yield = 290 mg, 91%).

Separation of the diastereomers: Acetonitrile (7 mL) was added to a round-bottom flask containing [**4c**][Δ-**2**]$_2$ (280 mg). The flask was cooled to 4 °C for 1 h, and the resulting precipitate was filtered and washed with Et$_2$O to afford [*P*-**4c**][Δ-**2**]$_2$ as a yellow solid (yield = 105 mg, ≈38%, d.r. = 94:6). After evaporation to dryness of the mother liquor, [*M*-**4c**][Δ-**2**]$_2$was obtained as a yellow solid (yield = 155 mg, ≈55%, d.r. = 70:30).

[P-4c][Δ-2]$_2$: Yellow solid; *de* = 88%; m.p. 245–250 °C; $[\alpha]_D^{20}=-65$ (*c* = 0.1, CH$_3$CN); ^{1}H NMR (400 MHz, [D$_6$]DMSO): $\delta=9.30$ (d, 2H, $J=$ 6.3 Hz), 8.53 (d, 2H, $J=6.3$ Hz), 8.45 (d, 2H, $J=1.8$), 7.96 (d, 4H, $J=$ 8.0 Hz, 2), 7.84 (d, 4H, $J=8.8$ Hz, 2), 7.54 (m, 4H), 7.40 (m. 4H, 2), 7.28 (d, 8H, $J=3.5$ Hz, 2), 6.56 (d, 4H, $J=8.8$ Hz, 2), 5.81 (d, 2H, $J=$ 15.9 Hz), 5.44 (d, 2H, $J=15.6$ Hz), 1.43 ppm (s, 18H); ^{13}C NMR (100 MHz, [D$_6$]DMSO): $\delta=172.1$ (C^{IV}), 151.8 (C^{IV}, d, $J=12.9$ Hz, 2), 147.1 (CH), 144.4 (C^{IV}), 142.6 (C^{IV}, d, $J=5.5$ Hz, 2), 142.1 (C^{IV}, d, $J=$ 9.2 Hz, 2), 131.8 (C^{IV}), 131.5 (C^{IV}, 2), 130.0 (C^{IV}, 2), 129.9 (CH), 129.2 (CH, 2), 128.5 (CH), 128.3 (CH, 2), 127.3 (CH), 126.3 (CH, 2), 125.7 (CH, 2), 124.1 (CH, 2), 122.5 (C^{IV}), 122.3 (CH, d, $J=2.8$ Hz, 2), 121.4 (C^{IV}, 2), 119.9 (C^{IV}, 2), 112.8 (C^{IV}, d, $J=14.7$ Hz, 2), 112.7 (C^{IV}, d, $J=$ 13.8 Hz, 2), 60.4 (CH$_2$), 37.0 (C^{IV}), 29.5 ppm (CH$_3$); ^{31}P NMR (162 MHz, [D$_6$]DMSO): $\delta=-83.41$ ppm; IR (neat): $\tilde{\nu}=$3054, 2970, 1622, 1450, 1234, 991, 816 cm^{-1}; UV/Vis (CH$_3$CN, 10^{-5} M): λ_{max} (ε) = 230 (2.14×10^5), 275 (1.79×10^5), 329 nm (1.7×10^4); CD (CH$_3$CN, 10^{-5} M): λ ($\Delta\varepsilon$) = 233 (309.7), 245 (−174.4), 264 (54.4), 301 (−24.5), 322 (−8.4), 330 cm^{2}mmol^{-1} (−14.8); MS (ES$^-$): *m*/*z* (%): 807.0 (100) BINPHAT; MS (ES$^+$): *m*/*z*

(%): 235.9 (100), 239.1 (67) [$M-C_8H_8-2CH_3$], 252.9 (73) [$M-C_8H_8-CH_3$], 269 (53) [$M-C_8H_8+1$], 186.1 (23) [$M/2$].

*[P-**4c**][PF$_6$]$_2$*: The compound was obtained as a white solid (yield = 96%, *ee* = 88%) by using the general procedure of exchange of anions **2** to PF_6. M.p. 220°C; $[\alpha]_D^{20} = -159$ ($c = 0.1$, H_2O); ^{1}H NMR (400 MHz, $CDCl_3$/[D_6]DMSO 14%): $\delta = 9.14$ (s, 2H), 8.24 (s, 2H), 8.01 (s, 2H), 7.36 (s, 2H), 7.22 (s, 2H), 5.77 (d, 2H, $J = 15.1$ Hz), 5.00 (d, 2H, $J = 14.9$ Hz), 1.26 ppm (s, 18H); ^{13}C NMR (100 MHz, [D_6]DMSO): $\delta = 172.1$ (C^{IV}), 147.1 (CH), 144.4 (C^{IV}), 131.6 (C^{IV}), 130.9 (CH), 129.9 (CH), 128.5 (CH), 127.3 (CH), 60.4 (CH_2), 37.0 (C^{IV}), 29.5 ppm (CH_3); IR (neat): $\tilde{\nu} = 2975$, 1628, 1454, 1424, 1373, 827 cm^{-1}; UV/Vis (CH_2Cl_2, 10^{-5} M): λ_{max} (ε) = 227 (3.8×10^4), 237 (2.9×10^4), 274 nm (2.1×10^4); CD (CH_2Cl_2, 10^{-5} M): λ ($\Delta\varepsilon$) = 219 (−19.0), 249 (8.3), 263 (3.6), 276 cm^2 mmol^{-1} (9.8); MS (ES$^+$): *m/z* (%): 239.1 (90) [$M-C_8H_8-2CH_3$], 252.9 (100) [$M-C_8H_8-CH_3$], 268.7 (86) [$M-C_8H_8+1$], 186.6 (100) [$M/2$].

*(+)-[M-**4c**][PF$_6$]$_2$*: The compound was obtained by resolution with Λ-BINPHAT. *ee* = 88%; $[\alpha]_D^{20} = +161$ ($c = 0.1$, H_2O).

Ion metathesis with Δ-TRISPHAT: A solution of [**4c**][I]$_2$ (85.0 mg, 0.136 mmol) in CH_2Cl_2/MeOH 4:1 (2 mL) was added to a solution of [cinchonidinium][Δ-**3**] (303.2 mg, 0.285 mmol) in acetone (4 mL). The mixture was stirred for about 5 min and then was evaporated to dryness. The diastereomeric salts were obtained after chromatography over basic alumina with CH_3CN as the eluent with a 1.2:1 ratio (yield = 55% of [*P*-**4c**][Δ-**3**]$_2$ and 45% of [*M*-**4c**][Δ-**3**]$_2$) as yellow solids (determined by ^{1}H NMR spectroscopic analysis in a mixture of CD_3CN (3%) in $CDCl_3$).

Separation of the diastereomers: CH_3CN (≈5 mL) was added to a round-bottom flask containing [**4c**][Δ-**3**]$_2$ (210 mg) until complete solubilization occurred. The flask was cooled to −20°C for a 30 min period. The yellow precipitate was filtered to afford [*P*-**4c**][Δ-**3**]$_2$ as a yellow solid (yield = 110 mg, ≈52%, d.r. > 98:2). After evaporation to dryness, [*M*-**4c**][Δ-**3**]$_2$ was obtained as a yellow solid (yield = 90 mg, ≈43%, d.r. = 97.5:2.5).

*[P-**4c**][Δ-**3**]$_2$*: Yellow solid; d.r. > 98:2; m.p. 300°C; $[\alpha]_D^{20} = -357.7$ (c = 0.1, CH_3CN); ^{1}H NMR (400 MHz, $CDCl_3$/CD_3CN 3%): $\delta = 9.95$ (d, 2H, $J = 6.6$ Hz), 8.22 (d, 2H, $J = 2.3$ Hz), 8.08 (dd, 2H, $J = 2.0$ Hz and 6.6 Hz), 7.67 (dd, 2H, $J = 3.7$ Hz and 5.3 Hz), 7.11 (dd, 2H, $J = 3.7$ Hz and 5.3 Hz), 6.46 (d, 2H, $J = 16.0$ Hz), 5.27 (d, 2H, $J = 16.0$ Hz), 1.51 ppm (s, 18H); ^{13}C NMR (75 MHz, [D_6]DMSO): $\delta = 172.6$ (C^{IV}), 147.5 (CH), 144.9 (C^{IV}), 141.6 (d, C^{IV}, $J = 6.5$ Hz), 132.0 (CH), 131.4 (C^{IV}), 130.4 (CH), 128.9 (CH), 127.8 (CH), 122.6 (C^{IV}), 113.6 (d, C^{IV}, $J = 20.0$ Hz), 60.9 (CH_2), 37.4 (C^{IV}), 29.9 ppm (CH_3); ^{31}P NMR (162 MHz, [D_6]DMSO): $\delta = -81.25$ ppm; IR (neat): $\tilde{\nu} = 2972$, 1622, 1444, 1389, 1235, 989, 818 cm^{-1}; UV/Vis (CH_3CN, 10^{-5} M): λ_{max} (ε) = 216 (2.45×10^5), 300 (1.9×10^4), 399 nm (1×10^3); CD (CH_3CN, 10^{-5} M): λ ($\Delta\varepsilon$) = 212 (307.2), 223 (−298.7), 236 (−84.7), 243 (−95.7), 285 (−4.4), 300 cm^2 mmol^{-1} (−6.1); MS (ES$^-$): *m/z* (%): 768.5 (100) TRISPHAT; MS (ES$^+$): *m/z* (%): 239.1 (90) [$M-C_8H_8-2CH_3$], 252.9 (100) [$M-C_8H_8-CH_3$], 268.7 (86) [$M-C_8H_8+1$], 186.6 (100) [$M/2$].

*[M-**4c**][Δ-**3**]$_2$*: Yellow solid; d.r. = 97.5:2.5; m.p. 285°C; $[\alpha]_D^{20} = -335.6$ (c = 0.1 in CH_3CN); ^{1}H NMR (400 MHz, $CDCl_3$/CD_3CN 3%): $\delta = 9.15$ (d, 2H, $J = 6.5$ Hz), 8.29 (d, 2H, $J = 2.0$ Hz), 8.26 (dd, 2H, $J = 2.0$ Hz and 6.3 Hz), 7.42 (s, 4H), 6.07 (d, 2H, $J = 16.2$ Hz), 5.32 (d, 2H, $J = 16.2$ Hz), 1.45 ppm (s, 18H); ^{13}C NMR (75 MHz, [D_6]DMSO): $\delta = 173.2$ (C^{IV}), 147.5 (CH), 145.1 (C^{IV}), 143.9 (CH), 141.7 (d, C^{IV}, $J = 6.5$ Hz), 132.0 (CH), 131.5 (C^{IV}), 130.3 (CH), 128.8 (CH), 127.7 (CH), 122.3 (C^{IV}), 113.2 (d, C^{IV}, $J = 20.0$ Hz), 59.5 (CH_2), 35.5 (C^{IV}), 27.9 ppm (CH_3); ^{31}P NMR (162 MHz, [D_6]DMSO): $\delta = -81.05$ ppm; IR (neat): $\tilde{\nu} = 2974$, 1624, 1445, 1389, 1235, 989, 818 cm^{-1}; UV/Vis (CH_3CN, 10^{-5} M): λ_{max} (ε) = 213 (3.05×10^5), 300 (3.0×10^4), 398 nm (1×10^3); CD (CH_3CN, 10^{-5} M): λ (ε) = 208 (236.1), 225 (−251.4), 236 (−114.8), 243 (−128.8), 278 (−6.4), 300 cm^2 mmol^{-1} (−8.4); MS (ES$^-$): *m/z* (%): 768.5 (100) TRISPHAT; MS (ES$^+$): *m/z* (%): 239.1 (97) [$M-C_8H_8-2CH_3$], 252.9 (100) [$M-C_8H_8-CH_3$], 268.8 (87) [$M-C_8H_8+1$], 186.3 (23) [$M/2$].

General procedure for the ion exchange of TRISPHAT anions to PF$_6$: Excess anhydrous $FeCl_3$ (46.7 mg, 0.288 mmol) was added to a solution of [*P*-**4c**][Δ-**3**]$_2$ (55 mg, 0.029) in dichloromethane (4 mL) at 0°C and stirred for 2 min. The mixture was washed with a saturated aqueous solution of KPF_6 (4 mL) and, after decantation and separation, the organic phase was further filtered over Celite. Finally, the desired (−)-[*P*-**4c**][PF_6]$_2$ salt was precipitated upon addition of Et_2O to the filtrate, before it was filtered and thoroughly washed with Et_2O and pentane. The desired compound was obtained as a white powder (14 mg, 73%). Enantiomeric excess was determined by ^{1}H NMR spectroscopy (the analysis was carried out in a mixture of [D_6]DMSO (14%) in $CDCl_3$) by using salt [nBu$_4$N][Δ-**2**] as the NMR chiral solvating agent.

*(−)-[P-**4c**][PF$_6$]$_2$*: White powder; *ee* = 90%; $[\alpha]_D^{20} = -162$ (c = 0.1, water).

*Crystal structure determination of [P-**4c**][Δ-**3**]$_2$*: CCDC-747488 (**[P-4c]-[Δ-3]$_2$**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Acknowledgements

We are grateful for financial support of this work by the Département d'Instruction Publique (Geneva), the Swiss National Science Foundation and the State Secretariat for Education and Research in particular. We would also like to thank Dr. Céline Besnard for her help in the production of the crystallographic drawings.

[1] R. F. Homer, T. E. Tomlinson, *Nature* **1959**, *184*, 2012–2013; K. Tsukahara, R. G. Wilkins, *J. Am. Chem. Soc.* **1985**, *107*, 2632–2635; R. P. Thummel, F. Lefoulon, S. Chirayil, V. Goulle, *J. Org. Chem.* **1988**, *53*, 4745–4747; M. Kuzuya, S. Kondo, K. Murase, *J. Phys. Chem.* **1993**, *97*, 7800–7802; S. H. R. Brienne, P. D. W. Boyd, P. Schwerdtfeger, G. A. Bowmaker, R. P. Cooney, *J. Mol. Struct.* **1995**, *356*, 81–94; B. J. Coe, N. R. M. Curati, E. C. Fitzgerald, *Synthesis* **2006**, 146.

[2] R. F. Homer, T. E. Tomlinson, *J. Chem. Soc.* **1960**, 2498–2503.

[3] L. A. Summers, *The Bipyridinium Herbicides*, Academic Press, New York, **1980**.

[4] B. L. Allwood, F. H. Kohnke, A. M. Z. Slawin, J. F. Stoddart, D. J. Williams, *J. Chem. Soc. Chem. Commun.* **1985**, 311–314.

[5] T. Klumpp, M. Linsenmann, S. L. Larson, B. R. Limoges, D. Bürssner, E. B. Krissinel, C. M. Elliott, U. E. Steiner, *J. Am. Chem. Soc.* **1999**, *121*, 1076; M. Vitale, N. B. Castagnola, N. J. Ortins, J. A. Brooke, A. Vaidyalingam, P. K. Dutta, *J. Phys. Chem. B* **1999**, *103*, 2408–2416; Y. Kim, H. Lee, P. K. Dutta, A. Das, *Inorg. Chem.* **2003**, *42*, 4215–4222; Y.-H. Kim, A. Das, H.-Y. Zhang, P. K. Dutta, *J. Phys. Chem. B* **2005**, *109*, 6929.

[6] I. Nunn, B. Eisen, R. Benedix, H. Kisch, *Inorg. Chem.* **1994**, *33*, 5079–5085; I. Unamuno, J. M. Gutiérrez-Zorrilla, A. Luque, P. Román, L. Lezama, R. Calvo, T. Rojo, *Inorg. Chem.* **1998**, *37*, 6452; P. Vitoria, J. I. Beitia, J. M. Gutiérrez-Zorrilla, E. R. Sáiz, A. Luque, M. Insausti, J. J. Blanco, *Inorg. Chem.* **2002**, *41*, 4396.

[7] B. J. Coe, L. A. Jones, J. A. Harris, I. Asselberghs, K. Wostyn, K. J. Clays, A. P. Persoons, B. S. Brunschwig, J. Garin, J. Orduna, *Proc. SPIE-Int. Soc. Opt. Eng.* **2003**, *5212*, 122–136; B. J. Coe, J. A. Harris, B. S. Brunschwig, J. Garin, J. Orduna, *J. Am. Chem. Soc.* **2005**, *127*, 3284–3285.

[8] F. Knoch, G. Schmauch, H. Kisch, *Z. Kristallogr.* **1995**, *210*, 225–225.

[9] I. C. Calder, T. M. Spotswood, C. I. Tanzer, *Aust. J. Chem.* **1967**, *20*, 1195–1212.

[10] F. Vögtle, D. Bombach, *Chem. Ber.* **1975**, *108*, 1682–1693.

[11] R. P. Thummel, F. Lefoulon, R. Mahadevan, *J. Org. Chem.* **1985**, *50*, 3824–3828; C. Campa, J. Camps, J. Font, P. De March, *J. Org. Chem.* **1987**, *52*, 521–525.

[12] C. Pasquini, V. Desvergnes-Breuil, J. J. Jodry, A. Dalla Cort, J. Lacour, *Tetrahedron Lett.* **2002**, *43*, 423–426.

[13] P. Pfeiffer, K. Quehl, *Chem. Ber.* **1931**, *64*, 2667–2671; B. Norden, F. Tjerneld, *FEBS Lett.* **1976**, *67*, 368–370; S. Kirschner, N. Ahmad, C. Munir, R. J. Pollock, *Pure Appl. Chem.* **1979**, *51*, 913–923; M. M. Green, C. Khatri, N. C. Peterson, *J. Am. Chem. Soc.* **1993**, *115*, 4941–4942; R. M. Yeh, M. Ziegler, D. W. Johnson, A. J. Terpin,

K. N. Raymond, *Inorg. Chem.* **2001**, *40*, 2216–2217; B. Laleu, G. Bernardinelli, R. Chauvin, J. Lacour, *J. Org. Chem.* **2006**, *71*, 7412–7416; O. Winkelmann, D. Linder, J. Lacour, C. Näther, U. Lüning, *Eur. J. Org. Chem.* **2007**, 3687–3697; C. Bonnot, J. C. Chambron, E. Espinosa, R. Graff, *J. Org. Chem.* **2008**, *73*, 868–881.

[14] J. Lacour, A. Londez, C. Goujon-Ginglinger, V. Buss, G. Bernardinelli, *Org. Lett.* **2000**, *2*, 4185–4188.

[15] J. Lacour, C. Ginglinger, C. Grivet, G. Bernardinelli, *Angew. Chem.* **1997**, *109*, 660–662; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 608–610; F. Favarger, C. Goujon-Ginglinger, D. Monchaud, J. Lacour, *J. Org. Chem.* **2004**, *69*, 8521–8524.

[16] J. Lacour, R. Frantz, *Org. Biomol. Chem.* **2005**, *3*, 15–19.

[17] J. Lacour, D. Linder, *Chem. Rec.* **2007**, *7*, 275–285; J. Lacour, D. Moraleda, *Chem. Commun.* **2009**, 7073–7089.

[18] B. Pégot, G. Vo-Thanh, D. Gori, A. Loupy, *Tetrahedron Lett.* **2004**, *45*, 6425–6428; C. Baudequin, D. Bregeon, J. Levillain, F. Guillen, J. C. Plaquevent, A. C. Gaumont, *Tetrahedron: Asymmetry* **2005**, *16*, 3921–3945; J. Ding, D. W. Armstrong, *Chirality* **2005**, *17*, 281–292; J. Ding, V. Desikan, X. X. Han, T. L. Xiao, R. F. Ding, W. S. Jenks, D. W. Armstrong, *Org. Lett.* **2005**, *7*, 335–337; R. Gausepohl, P. Buskens, J. Kleinen, A. Bruckmann, C. W. Lehmann, J. Klankermayer, W. Leitner, *Angew. Chem.* **2006**, *118*, 3772–3775; *Angew. Chem. Int. Ed.* **2006**, *45*, 3689–3692; T. Hashimoto, K. Maruoka, *Chem. Rev.* **2007**, *107*, 5656–5682; P. S. Schulz, N. Muller, A. Bosmann, P. Wasserscheid, *Angew. Chem.* **2007**, *119*, 1315–1317; *Angew. Chem. Int. Ed.* **2007**, *46*, 1293–1295; P. Wasserscheid, T. Welton, *Ionic Liquids in Synthesis 2*, Wiley-VCH, Weinheim, **2007**; Y. Matsuoka, Y. Ishida, D. Sasaki, K. Saigo, *Chem. Eur. J.* **2008**, *14*, 9215–9222.

[19] K. Mikami, K. Aikawa, Y. Yusa, J. J. Jodry, M. Yamanaka, *Synlett* **2002**, 1561–1578.

[20] L. Adriaenssens, L. Severa, T. Salova, I. Cisarova, R. Pohl, D. Saman, S. V. Rocha, N. S. Finney, L. Pospisil, P. Slavicek, F. Teply, *Chem. Eur. J.* **2009**, *15*, 1072–1076; A. Andronova, F. Szydlo, F. Teply, M. Tobrmanova, A. Volot, I. G. Stara, I. Stary, L. Rulisek, D. Saman, J. Cvacka, P. Fiedler, P. Vojtisek, *Collect. Czech. Chem. Commun.* **2009**, *74*, 189–215.

[21] L. Eshdat, E. Shabtai, S. A. Saleh, T. Sternfeld, M. Saito, Y. Okamoto, M. Rabinovitz, *J. Org. Chem.* **1999**, *64*, 3532–3537.

[22] E. L. Eliel, S. H. Wilen, *Stereochemistry of Organic Compounds*, 1st ed., Wiley, New York, **1994**; J. Jacques, A. Collet, S. H. Wilen, *Enantiomers, Racemates, and Resolutions*, 2nd ed., Krieger, Melbourne, **1994**.

[23] H. Amouri, R. Thouvenot, M. Gruselle, *C. R. Chim.* **2002**, *5*, 257–262; M. Chavarot, S. Menage, O. Hamelin, F. Charnay, J. Pecaut, M. Fontecave, *Inorg. Chem.* **2003**, *42*, 4810–4816; H. Amouri, R. Caspar, M. Gruselle, C. Guyard-Duhayon, K. Boubekeur, D. A. Lev, L. S. B. Collins, D. B. Grotjahn, *Organometallics* **2004**, *23*, 4338–4341; M. Gruselle, R. Thouvenot, W. Caspar, K. Boubekeur, H. Amouri, M. Ivanov, K. Tonsuaadu, *Mendeleev Commun.* **2004**, *14*, 282–283; O. Hamelin, J. Pecaut, M. Fontecave, *Chem. Eur. J.* **2004**, *10*, 2548–2554; L. Mimassi, C. Guyard-Duhayon, M. N. Rager, H. Amouri, *Inorg. Chem.* **2004**, *43*, 6644–6649; C. R. Brodie, J. R. Aldrich-Wright, *Eur. J. Inorg. Chem.* **2007**, 4781–4793; L. Mimassi, C. Cordier, C. Guyard-Duhayon, B. E. Mann, H. Amouri, *Organometallics* **2007**, *26*, 860–864; S. Bonnet, J. Li, M. A. Siegler, L. S. von Chrzanowski, A. L. Spek, G. van Koten, R. J. M. K. Gebbink, *Chem. Eur. J.* **2009**, *15*, 3340–3343.

[24] A. Auffrant, A. Barbieri, F. Barigelletti, J. Lacour, P. Mobian, J.-P. Collin, J.-P. Sauvage, B. Venturi, *Inorg. Chem.* **2007**, *46*, 6911–6919.

[25] J. Lacour, S. Barchechath, J. J. Jodry, C. Ginglinger, *Tetrahedron Lett.* **1998**, *39*, 567–570; L. Vial, J. Lacour, *Org. Lett.* **2002**, *4*, 3939–3942; J. Vachon, C. Pérollier, D. Monchaud, C. Marsol, K. Ditrich, J. Lacour, *J. Org. Chem.* **2005**, *70*, 5903–5911.

[26] J. Lacour, S. Torche-Haldimann, J. J. Jodry, *Chem. Commun.* **1998**, 1733–1734; D. Monchaud, J. J. Jodry, D. Pomeranc, V. Heitz, J.-C. Chambron, J.-P. Sauvage, J. Lacour, *Angew. Chem.* **2002**, *114*, 2423–2425; *Angew. Chem. Int. Ed.* **2002**, *41*, 2317–2319; R. Frantz, A. Pinto, S. Constant, G. Bernardinelli, J. Lacour, *Angew. Chem.* **2005**, *117*, 5188–5192; *Angew. Chem. Int. Ed.* **2005**, *44*, 5060–5064.

[27] Verified in ^{1}H NMR spectroscopy by using salt [Bu_4N][Δ-**2**] as the NMR chiral solvating agent.

[28] K. Mislow, E. Simon, M. A. W. Glass, G. H. Wahl, H. B. Hopps, *J. Am. Chem. Soc.* **1964**, *86*, 1710–1733; L. Loncar-Tomascovic, R. Sarac-Arneri, A. Hergold-Brundic, A. Nagl, M. Mintas, J. Sändstrom, *Helv. Chim. Acta* **2000**, *83*, 479–494; J. Sandström, *Chirality* **2000**, *12*, 162–171.

[29] M. Hofbauer, M. Mobius, F. Knoch, R. Benedix, *Inorg. Chim. Acta* **1996**, *247*, 147–154.

[30] G. Schmauch, F. Knoch, H. Kisch, *Chem. Ber.* **1995**, *128*, 303–307.

[31] F. Knoch, G. Schmauch, H. Kisch, *Z. Kristallogr.* **1995**, *210*, 76–77.

Received: September 16, 2009
Published online: January 22, 2010

