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Configurational Ordering of Cationic Chiral Dyes Using a Novel C_2-Symmetric Hexacoordinated Phosphate Anion

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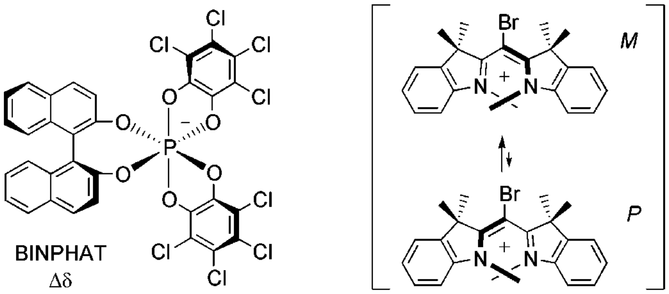
ABSTRACT



C_2-Symmetry hexacoordinated phosphorus BINPHAT anion—of configuration controlled by a BINOL ligand—can be prepared readily in a one-pot process and behaves as an efficient NMR chiral shift agent and chiral inducer onto monomethinium dyes (CD, ^{1}H NMR).

The induction of optical activity by chiral substances acting on achiral or racemic substrates is an important phenomenon.[1] Optically active counterions can induce optical activity onto configurationally labile ionic species in solution (Pfeiffer Effect). The interaction of chiral anions (tartrate, borate) with cationic chiral dyes and transition metal complexes has been studied in particular.[2] Of most relevance to the current work is the observation by Owen and Schuster that a chiral borate anion forms penetrated ion pairs with chiral cationic cyanine dyes leading to induced circular dichroism (CD) spectra.[2b] Unfortunately, in most of these studies, the magnitude of the induction (diastereoselectivity) is not known and the efficiency of the chiral inducers is difficult to appreciate and quantify. Herein, we report the synthesis of a novel C_2-symmetric hexacoordinated phosphate anion of configuration controlled by the chiral BINOL[3] ligand **1** (de > 96%). An asymmetric induction from this anion onto chiral dyes **2a** and **2b** was observed by CD and ^{1}H NMR spectroscopy—the latter allowing a quantitative determination of the selectivity of the induction.

We recently reported the synthesis and resolution of the D_3-symmetric tris(tetrachlorobenzenediolato)phosphate(V) anion **3** (or TRISPHAT).[4] This anion is an efficient NMR chiral shift reagent and a chiral inducer for iron(II) tris-

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(bisimine) complexes.[5c] This initial study prompted us to investigate the generality of the asymmetric induction by **3**, particularly onto chiral C_2-symmetric monomethinium dyes **2a** and **2b** (Figure 1).[6] Salts [**2a**][Δ-**3**] and [**2b**][Δ-**3**] were prepared by mixing [cinchonidinium][Δ-**3**] and [**2a**,**b**][BF_4^-] in CH_2Cl_2 and isolated by chromatography over silica gel (CH_2Cl_2, 70−85%).[5d]

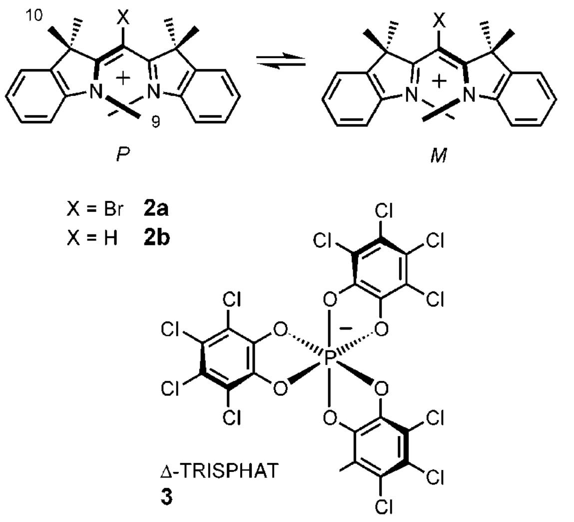


Figure 1. Chiral monomethinium dyes **2a** and **2b** and TRISPHAT anion **3**.

Unfortunately, ^1H NMR and CD analyses revealed that **3** is a very poor NMR chiral shift reagent and does not behave as a chiral inducer for these substrates (Figure 2, spectrum b). Assuming that the D_3-symmetry of anion **3** was not adapted for the chiral recognition of such C_2-symmetric cations, we decided to investigate the synthesis of C_2-symmetric hexacoordinated phosphate anions. Furthermore, the introduction of a well-chosen C_2-symmetric chiral ligand, along with two tetrachlorocatechols **4**,[7] should permit a diastereoselective synthesis by predetermination of the configuration[8] around the phosphorus atom. There was to our knowledge only one example of a hexacoordinated phosphate anion bearing one chiral ligand, (−)-mandelic acid, along with two pyrocatechol rings, but it is configurationally labile and epimerizes in solution to give a 55:45 mixture of diastereomers.[9]

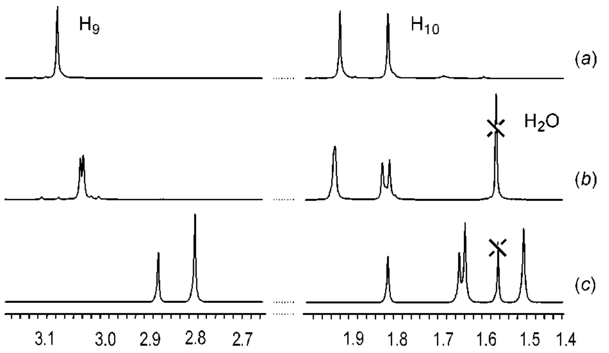
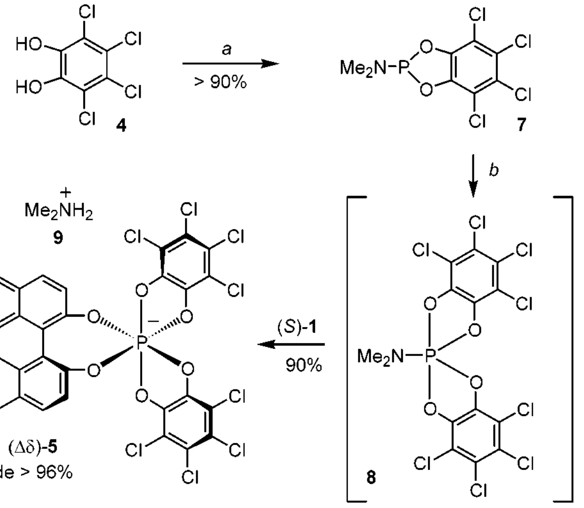


Figure 2. ^1H NMR spectra (400 MHz, $CDCl_3$, parts) for (*a*) [**2a**][BF_4^-], (*b*) [**2a**][Δ-**3**], de 0%, and (*c*) [**2a**][Λ-**5**], de 27%.

The synthesis of bis(tetrachlorobenzenediolato)mono([1,1′]-binaphthalenyl-2,2′-diolato)phosphate(V) anion **5** (or BINPHAT) was effected via a three-step one-pot procedure: **4** and tris(dimethylamino)phosphine **6** were heated together in toluene with a catalytic amount of NH_4Cl (2 mol %) to afford aminophosphine **7** in high yield (>95%). Oxidation of **7** at room temperature with *o*-chloranil in the presence of [1,1′]-binaphthalenyl-2,2′-diol **1** (racemic or enantiopure) in CH_2Cl_2 yielded the desired phosphate anion **5**, which precipitated spontaneously as its dimethylammonium salt in a 90% yield. The synthesis probably proceeds via spirophosphorane **8**, as *o*-chloranil easily oxidizes **7** to **8** (Scheme 1).[10] ^1H and ^{31}P NMR data suggested the presence of only one diastereomer, with no trace of any other diastereomer being detected either in the precipitate or in the mother liquor.

Scheme 1. One-Pot Synthesis of BINPHAT Anion



[a] **6** (1.7 equiv for 1.7 equiv of **4**), NH_4Cl (2 mol %), toluene, reflux. [b] *o*-Chloranil (1.7 equiv), **1** (1.0 equiv), CH_2Cl_2, 20 °C.

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(7) Tetrachlorocatechol was preferred to pyrocatechol as studies on **3** showed that the electron-withdrawing chlorine atoms enhance both the chemical and the configurational stability of the anion.

The precipitate sometimes contained small amounts of *rac*-**3** ($<$10%), which could not be removed by recrystallization since **5** is unstable in solution (except in MeOH) when associated with acidic $Me_2NH_2^+$ counterion **9**. However, exchanging **9** for nonacidic monomethinium cations **2a** and **2b**, yielding in all cases stable ion pairs, could easily overcome this difficulty.[11] During the chromatography we were able to separate [**2a**,**b**][**5**] from [**2a**,**b**][**3**], since the salts containing TRISPHAT **3** migrate faster than those containing BINPHAT **5**.[5d]

Crystals of salt (+)-[**2b**][**5**], prepared using an anion made from (*R*)-**1**, were obtained by diffusion of hexane in EtOAc, permitting an analysis by low-temperature X-ray diffraction, which confirmed the presence of a single diastereomer of **5**.[12] The configuration of the BINPHAT anion derived from (*R*)-**1** was found to be $\Lambda\lambda$ (Figure 3).[13] The use of enantiopure **1** thus enabled us to obtain enantiopure **5** readily. This is the first example of complete predetermination of chirality by a single chiral bidentate ligand on a phosphorus atom in octahedral geometry bearing three bidentate ligands. Another interesting feature of this X-ray analysis is the perfect asymmetric induction of Λ-**5** onto **2b** as only diastereomeric [*P*-**2b**][Λ-**5**] salt crystallizes. However, despite large uncertainties on the final geometrical parameters—due to the low data/parameter ratio—an analysis of the crystal packing does not reveal any particular favorable interactions between the ions.

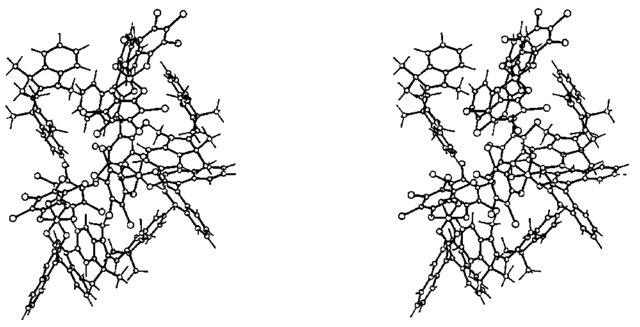

Figure 3. Stereoview of the asymmetric unit containing three distinct cations *P*-**2b** and three anions $\Lambda\lambda$-**5** derived from (*R*)-**1**.

The asymmetric induction of **5** onto monomethinium cations **2a** and **2b** in solution was studied both by ^{1}H NMR and CD spectroscopy. For salt [**2a**][Λ-**5**], two sets of signals for the nonaromatic protons of each enantiomer are observed at room temperature (Figure 2, spectrum c).[14]

Rather large differences in chemical shifts ($\Delta\Delta\delta$) are obtained for the H(9) (0.09 ppm) and the H(10) protons (0.18 and 0.15 ppm), showing that the BINPHAT anion **5**, contrary to TRISPHAT **3**, acts as a powerful NMR chiral shift reagent. This is the first example of observation by NMR of an asymmetric induction in this family of dyes. By integration of the respective signals, we determined diastereoselectivities of about 27% in $CDCl_3$ and 40% in C_6D_6. In the case of salt [**2b**][Λ-**5**], a low-temperature experiment was required, since the interconversion energy is low, and the *P* and *M* enantiomers of **2b** are not distinguishable at 21 °C.[14]

Cooling the NMR sample to −60 °C allowed us to see two sets of signals for the H(9) protons corresponding to each enantiomer. By integration of the respective signals, we determined a 30% de.

CD analyses of solutions of [**2b**][Λ-**5**] in different solvents ($CHCl_3$, toluene) reveal a strong negative induced spectrum for the cyanine band around 450 nm (Figure 4), indicating that the preferred association is with the *P*-helical form of the dye.[15] In both solvents, the CD spectra are temperature-dependent but concentration-independent, thus eliminating aggregation as the cause of the induction. Salts [**2a**][Λ-**5**] revealed at 21 °C similar negative induced CD spectra at 520 nm ($\Delta\epsilon = -4.3$).

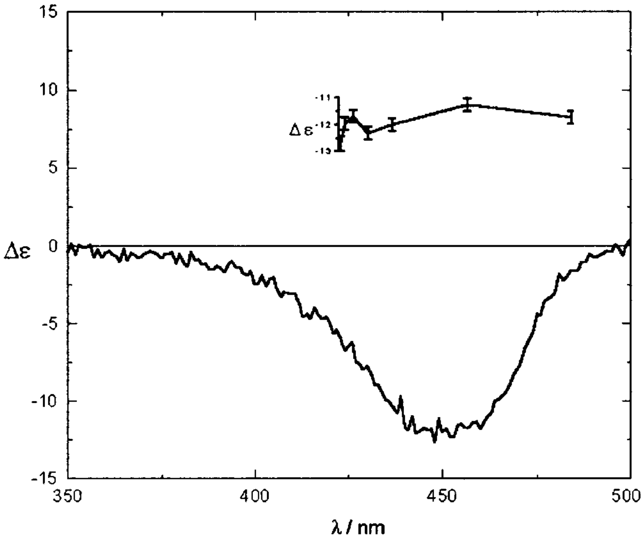

Figure 4. CD spectra of [**2b**][Λ-**5**] at room temperature in toluene, $c = 8.5 \times 10^{-4}$ M. Inset: $\Delta\epsilon$ at 450 nm as a function of concentration. The errors bars correspond to concentrations of (from right) 8.5, 4.7, 2.0, 1.1, 0.59, 0.29, and 0.13 × 10^{-4} M.

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(11) The cation exchange proceeds similarly for **5** and **3**, however, using basic alumina instead of silica gel. See ref 5d.

(12) The asymmetric unit contains three pairs of cations and anions and four molecules of EtOAc. All the anions and cations have identical configuration, respectively. Crystallographic data are available as Supporting Information.

(13) Δ or Λ corresponds to the configuration of the P-center and δ or λ to the conformational isomerism of the BINOL ligand.

(14) Interconversion energies are 22.7 and 11.9 kcal mol^{-1} for [**2a**][BF_4^-] and [**2b**][BF_4^-]. Coalescence temperatures (^{1}H NMR, 400 MHz) are 151 and −44 °C, respectively. See ref 6b.

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We conclude that the monomethinium dyes and BINPHAT anion form diastereomeric ion pairs of unequal energies in favor of the [*P*-**2a**][Λ-**5**] and [*P*-**2b**][Λ-**5**]. The importance of the symmetry (C_2 vs D_3) of the chiral anion is demonstrated for chiral inducing as well as NMR chiral shift properties.

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Supporting Information Available: Spectral data for compounds [**9**][**5**] and [**2a**,**b**][**5**] and X-ray crystallographic data for (+)-[**2b**][**5**]. This material is available free of charge via the Internet at http://pubs.acs.org.

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