TRISPHAT-N: A Chiral Hexacoordinated Phosphate Anion with Unique Asymmetric Coordinating Properties

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Summary: A simple and efficient chiral anionic N-ligand: the introduction of a Lewis basic nitrogen onto the TRISPHAT skeleton allows the direct and efficient stereocontrol of tropos chiral ligands bound to metal complexes or of stereogenic metal centers (dr up to 96:4).

Recently, the chemistry of chiral hexacoordinated phosphate anions has been revitalized, as anions such as tris(tetrachlorobenzenediolato)phosphate(V) (**1**; TRISPHAT, Λ or Δ enantiomer)[1] have been shown to be valuable chiral NMR solvating, resolving, and asymmetry-inducing reagents for chiral cationic species.[2] However, effective chiral recognition was essentially achieved in solution only in associations with complementary D_3-symmetric metal complexes of the type [M(diimine)$_3$]$^{2+}$ (diastereomeric ratio (dr) > 90:10).[3,4] Efficient stereocontrol over the configuration of conformationally labile chiral ligands bound to metal centers was also never described using chiral anions as supramolecular chiral auxiliaries.[5]

We interpreted this lack of effective chiral recognition between **1** and most cationic metallic complexes as the result of the exclusive presence of ion pairs,[6] the chiral anion being positioned at a distance too far from the metal center or its ligands to interact efficiently.[7] Any modification of the anion structure that would ensure a tighter anion–cation association would then be beneficial. As cationic metal complexes are usually Lewis acidic, the introduction of a Lewis basic nitrogen atom on the skeleton

of the phosphate anion was deemed necessary. Lewis acid–Lewis base interactions would essentially ensure the formation of zwitterionic complexes and possibly induce stronger chiral recognition and asymmetric induction processes. In this context, we report herein the synthesis and resolution of the novel nitrogen-containing hexacoordinated phosphate anion **2**, denoted TRISPHAT-N, which can interact directly with metal centers and allow the stereocontrol of molecular events that previous non-coordinating chiral anions could not achieve.

To modify as little as possible the structural features of TRISPHAT, only one of the three tetrachlorocatecholate ligands was exchanged by a nitrogen-containing diol. 5-Chloropyridine-2,3-diol (**3**) was selected for its commercial availability and proven efficiency in metal binding events.[4d,8] The derived phosphate anion **2**, namely TRISPHAT-N, was prepared by following reported guidelines.[9] Anhydrous tetrachlorocatechol and P(NMe$_2$)$_3$ were reacted in toluene at reflux. After concentration in vacuo, successive additions in CH$_2$Cl$_2$ of *o*-chloranil (3,4,5,6-tetrachloro-3,5-cyclohexadiene-1,2-dione), **3**, and then [Bu$_3$NH][Cl] yielded the desired tri-*n*-butylammonium salt of racemic phosphate **2** (Scheme 1). The analytically pure compound [Bu$_3$NH][*rac*-**2**] was obtained after chromatography (yield 79%, 22 g scale, four consecutive steps).

The resolution of the anion was achieved by the addition of *N*-benzylcinchonidinium chloride salt ([**4**][Cl]; 1.0 equiv) to a CHCl$_3$ solution of [Bu$_3$NH][*rac*-**2**]. Selective precipitation of the diastereomerically pure (−)-[**4**][Δ-**2**] salt was afforded in good yield (46%).[10] The Λ enantiomer was isolated from the mother liquor as (+)-[Bu$_4$N][Λ-**2**] after ion exchange metathesis with [Bu$_4$N][Cl] and chromatography (SiO$_2$, CH$_2$Cl$_2$). The non-racemic anion **2** displayed in our hands good chemical and con-

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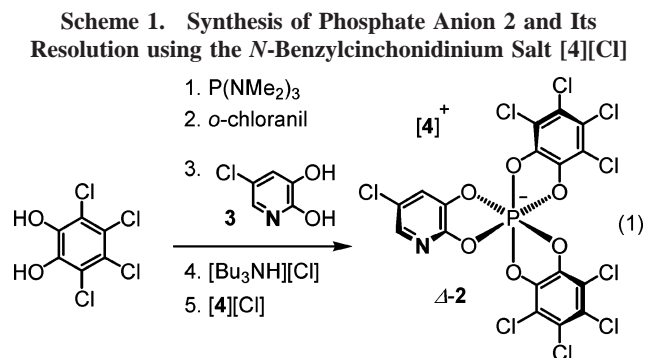
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(10) Circular dichroism analysis of salts (−)-[**4**][Δ-**2**] (MeOH, ∼10^{-6} M) reveals strong exciton coupling in the π–π* region with positive and negative Cotton effects at the lowest and highest wavelengths, confirming the Δ configuration: Bas, D.; Bürgi, T.; Lacour, J.; Vachon, J.; Weber, J. *Chirality* **2005**, *17*, S143–S148. Of course, the CD spectra of (+)-[Bu$_4$N]-[Λ-**2**] present the opposite situation.

Scheme 1.   Synthesis of Phosphate Anion 2 and Its Resolution using the *N*-Benzylcinchonidinium Salt [4][Cl]
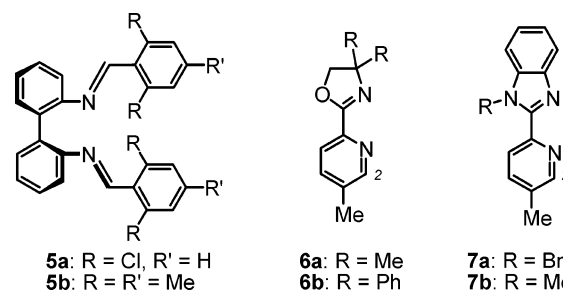

Figure 1. Ligands **5** (*tropos*, represented with *P* (S_a) conformation), **6** (pyridine oxazoline), and **7** (pyridine benzoimidazole).

figurational stability. No evidence of racemization could be found during, for instance, the ion exchange metathesis of cation **4** by Bu$_4$N$^+$. Monocrystals of the cinchonidinium derivative were obtained, and the absolute Δ configuration was determined by a crystal structure analysis.[11] P—O bond lengths and O—P—O bond angles are not so different from those measured for TRISPHAT (**1**),[12] although one P—O bond linked to the oxypyridonate unit—the one that involves the oxygen closest to the nitrogen atom—is much shorter (1.690 Å) than usual; the longest bond (1.723 Å) is the other P—O bond linked to the heterocycle.

The ability of anion **2** to form zwitterionic species and thus behave as ligand and chiral auxiliary together was first assessed in association experiments with Lewis acidic metal complexes bearing the chiral conformationally labile (*tropos*) ligands **5a** and **5b** (Figure 1),[13] our purpose being the stereocontrol of the absolute *P* or *M* geometry of the ligands. Salts [Cu(**5a**)(CH$_3$CN)$_2$][PF$_6$] and [CpRu(**5b**)(CH$_3$CN)][PF$_6$] were selected as precedents and indicated clearly that the biaryldiimine ligands **5a** and **5b** would adopt indeed atropoisomeric *P* and *M* conformations (S_a and R_a, respectively) at the vicinity of metal ions.[14,15]

The complex [Cu(**5a**)(Δ-**2**)] was prepared by ion exchange metathesis of [Cu(**5a**)(CH$_3$CN)$_2$][PF$_6$] and (−)-[**4**][Δ-**2**] and readily isolated by chromatography due to remarkable air and moisture stability for a 16-electron species and noticeable

lipophilicity (SiO$_2$, CH$_2$Cl$_2$, 72%).[16,17] NMR spectroscopic analysis (^{1}H, ^{13}C, and ^{31}P, CDCl$_3$, 293 K) revealed two sets of signals in a 66:34 ratio and a lack of coordinating CH$_3$CN ligand(s) upon ion exchange. These results indicated a coordination of the anion to the Cu center, resulting in two diastereomers, [Cu(*P*-**5a**)(Δ-**2**)] and [Cu(*M*-**5a**)(Δ-**2**)],[18] the exchange of anion Δ-**2** within the complexes being furthermore slow on the NMR time scale (as evidenced by ^{31}P NMR). The existence of a zwitterionic complex was furthermore confirmed by X-ray diffraction analysis of [Cu(**5a**)(Δ-**2**)], which crystallized as a single diastereomer in CH$_2$Cl$_2$/hexane; the biphenyldiimino ligand adopts a *P* (S_a) configuration in the solid state (Figure 2).[19]

Assuming that the relative lack of stereocontrol (dr 66:34) around the trigonal-planar Cu(I) atom was the result of overly distant interactions of ligands Δ-**2** and diimine **5a**, care was taken to study further systems based on more hindered pseudotetrahedral metal centers that would position the stereogenic elements closer together. For that purpose, the salt [CpRu(**5b**)(CH$_3$CN)][PF$_6$] was synthesized and treated with (−)-[**4**][Δ-**2**] and (+)-[Bu$_4$N][Λ-**2**]. The resulting complexes [CpRu(**5b**)(Δ-**2**)] and [CpRu(**5b**)(Λ-**2**)] were isolated using the already described chromatographic protocol (SiO$_2$, CH$_2$Cl$_2$, R_f = 0.82, 70−68%).[16] Only one set of signals was observed in NMR spectroscopy (^{1}H, ^{13}C, and ^{31}P), irrespective of the solvent used for the analyses (CD$_2$Cl$_2$, CDCl$_3$, C$_6$D$_6$, toluene-d_8).[20] CD spectra displayed intense Cotton effects in the visible MLCT region

(11) Crystal data for (−)-[**4**][Δ-**2**] ((C$_{17}$H$_2$Cl$_9$NO$_6$P)(C$_{26}$H$_{29}$N$_2$O)-(C$_3$H$_6$O)): M_r = 1109.9, orthorhombic, $P2_12_12_1$, a = 11.5179(5) Å, b = 19.1156(11) Å, c = 23.1645(11) Å, V = 5100.2(4) Å^3; Z = 4, μ = 0.580 mm^{-1}, d_{exptl} = 1.445 g cm^{-3}, Mo Kα radiation (λ = 0.710 73 Å), 64 539 reflections measured at 200 K, 9948 unique reflections, of which 4195 were observed ($|F_o| > 4\sigma(F_o)$). Data were corrected for Lorentz and polarization effects and for absorption (T_{min}, T_{max} = 0.8971, 0.9427). The structure was solved by direct methods (SIR97). All calculations were performed with the XTAL system. Full-matrix least-squares refinement based on F using weights of $1/(\sigma^2(F_o) + 0.0002(F_o^2))$ gave the final values R = 0.037, R_w = 0.034, and S = 1.65(2) for 636 variables. Flack parameter x = −0.02(9). CCDC-629076 contains the supplementary crystallographic data. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, U.K.; fax (+ 44) 1223-336-033; email deposit@ccdc.cam.ac.uk).

(12) TRISPHAT (**1**) adopts an octahedral geometry and a D_3 symmetry: i.e., all P—O bond lengths (1.714 Å) and O—P—O bond angles (90°) are identical.

(13) For a previous use of ligand **5b**, see: Costa, A. M.; Jimeno, C.; Gavenonis, J.; Carroll, P. J.; Walsh, P. J. *J. Am. Chem. Soc.* **2002**, *124*, 6929−6941. For a general review on the use of achiral ligands to convey asymmetry in enantioselective catalysis, see: Walsh, P. J.; Lurain, A. E.; Balsells, J. *Chem. Rev.* **2003**, *103*, 3297−3344.

(14) The salts [Cu(**5a**)(CH$_3$CN)$_2$][PF$_6$] and [CpRu(**5b**)(CH$_3$CN)][PF$_6$] were simply prepared by treatment of [Cu(CH$_3$CN)$_4$][PF$_6$] and [CpRu(CH$_3$CN)$_3$][PF$_6$] with the corresponding ligands **5a** and **5b**. For the preparation of ruthenium precursor, see: Kündig, E. P.; Monnier, F. R. *Adv. Synth. Catal.* **2004**, *346*, 901−904.

(15) The complex [Cu(**5a**)(CH$_3$CN)$_2$][PF$_6$] is reminiscent of catalysts used previously for enantioselective alkene aziridination reactions: Shi, M.; Wang, C.-J. *Chirality* **2002**, *14*, 412−416. Gillespie, K. M.; Sanders, C. J.; O'Shaughnessy, P.; Westmoreland, I.; Thickitt, C. P.; Scott, P. *J. Org. Chem.* **2002**, *67*, 3450−3458 and references therein.

(16) In a typical association experiment, a solution of [**4**][Δ-**2**] (0.138 mmol) in acetone (4 mL) was added at 20 °C to a solution of [Cu(**5a**)-(NCMe)$_2$][PF$_6$] (0.126 mmol) in dry N$_2$-saturated CH$_2$Cl$_2$ (5 mL). The resulting mixture was stirred for 5 min and then concentrated in vacuo. Chromatography of the residue (SiO$_2$, 1 × 7 cm, CH$_2$Cl$_2$) afforded [Cu-(**5a**)(Δ-**2**)] as a yellow solid (R_f = 0.91, 72%).

(17) The corresponding PF$_6$ and TRISPHAT salts are unstable. They are air- and moisture-sensitive and cannot be purified by chromatography (SiO$_2$).

(18) The atropoisomerism of ligands **5** was studied at low and high temperature by VT-NMR. Whereas no changes were observed at low temperature, the occurrence of stereodynamics (coalescence around 343 K of most signals) was monitored at elevated temperature for [Cu(**5a**)(Δ-**2**)]. See the Supporting Information.

(19) Crystal data for [Cu(*P*-**5a**)(Δ-**2**)] ((C$_{43}$H$_{18}$Cl$_{13}$CuN$_3$O$_6$P)(CHCl$_3$)$_2$): M_r = 1466.7, orthorhombic, $P2_12_12_1$, a = 14.4833(10) Å, b = 19.3609-(18) Å, c = 20.7455(13) Å, V = 5817.2(8) Å^3; Z = 4, μ = 1.323 mm^{-1}, d_{exptl} = 1.675 g cm^{-3}, Mo Kα radiation (λ = 0.710 73 Å), 72 581 reflections measured at 200 K, 11 264 unique reflections, of which 6024 were observed ($|F_o| > 4\sigma(F_o)$). Data were corrected for Lorentz and polarization effects and for absorption (T_{min}, T_{max} = 0.7810, 0.8366). The structure was solved by direct methods (SIR97). All calculations were performed with the XTAL system. Full-matrix least-squares refinement based on F using weights of $1/(\sigma^2(F_o) + 0.0002(F_o^2))$ gave final values R = 0.044, R_w = 0.040, and S = 1.46(1) for 677 variables; Flack parameter x = 0.00(3). CCDC-629067 contains the supplementary crystallographic data for **1**. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, U.K.; fax (+ 44) 1223-336-033; email deposit@ccdc.cam.ac.uk).

(20) Stereocontrol within "classical" diastereomeric ion pairs is usually highly dependent of the polarity of the solvent. See refs 3a,b and references therein.
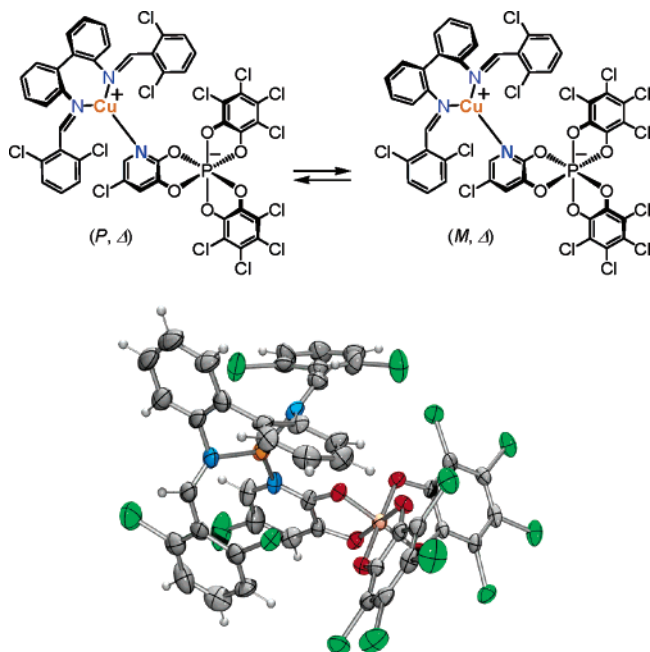
Figure 2. *tropos* ligands: solution equilibrium among diastereomeric Cu(I) complexes and X-ray crystal structure of the zwitterionic complex [Cu(*P*-**5a**)(Δ-**2**)]. Ellipsoids are represented at the 50% probability level.
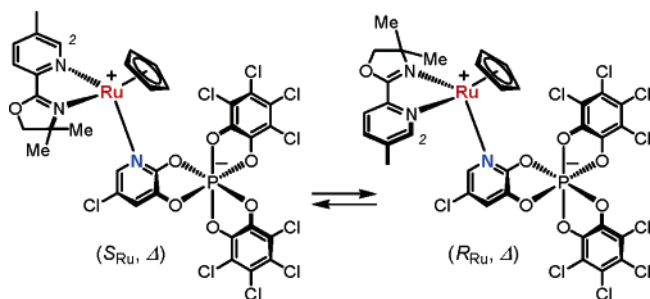

Figure 3. Chirality at metal: stereocontrol among (S_{Ru})-[CpRu-(**6a**)(Δ-**2**)] and (R_{Ru})-[CpRu(**6a**)(Δ-**2**)]. The priority sequence of the ligands is η^5-C$_5$H$_5$ > **2** > "imine" > pyridine.

with perfect mirror image symmetry (CH$_2$Cl$_2$, 4×10^{-5} M, $\Delta\epsilon_{397}$ +12 and -13 for [CpRu(**5b**)(Δ-**2**)] and [CpRu(**5b**)(Λ-**2**)], respectively), all data indicating the occurrence of a single zwitterionic complex in solution.

Having established that anion **2** can control effectively the conformation of *tropos* ligands bound to a metal center, we decided to study the possibility of controlling the configuration of the metal center itself using, as models, CpRu complexes of achiral ligands **6** and **7** (Figures 1 and 3). These compounds belong to the class of chiral organometallic half-sandwich complexes made of unsymmetrical bidentate ligands and arene metal fragments that have been strongly studied for their "chiral-at-metal" properties.[21] In the particular case of CpRu complexes bearing diimino ligands, however, there is to our knowledge only one report detailing the stereocontrol of the metal center by an enantiopure pyridine imine ligand; a moderate level of selectivity was achieved under kinetic control (dr 56:44).[22,23]

In view of this precedent, it was decided to study the stereocontrol of this challenging class of (η^5-C$_5$H$_5$)Ru moieties.

Table 1. Synthesis and Properties of [CpRu(ligand)(Δ-2)] Zwitterionic Complexes

ligand	yield (%)	dr[a]	dr[b]	$\Delta\delta_{max}$[b] (ppm)
6a	70	72:27	80:20	0.33
6b	71	89:11	91:09	0.73
7a	54	89:11	92:08	0.71
7b	60	95:05	96:04	0.70

[a] Conditions: ^{1}H NMR, 500 MHz, CD$_2$Cl$_2$. [b] Conditions: ^{1}H NMR, 500 MHz, toluene-d_8 + 5% CD$_3$NO$_2$.

The compounds [CpRu(**6**)(Δ-**2**)] and [CpRu(**7**)(Δ-**2**)] were prepared in a manner analogous to that for [CpRu(**5b**)(Δ-**2**)].[16] Slightly better yields were obtained for the formation of the oxazoline over the benzoimidazole derivatives (70−71% vs 54−60% from **6a**,**b** and **7a**,**b**, respectively).[24] Significantly, both ^{1}H and ^{13}C NMR spectra revealed the complete displacement of the acetonitrile ligands from the starting metal fragment. As expected, an efficient enantiodifferentiation was achieved in the presence of Δ-**2**, as dual sets of signals were obtained in both ^{1}H and ^{31}P NMR, the latter observation indicating slow exchange kinetics of the chiral ions on the NMR time scale. Of all the split signals, the higher frequency singlets of pyridine protons H2 (Figures 1 and 3) were particularly easy to monitor and very large differences in chemical shifts ($\Delta\delta_{max}$ up to 0.73 ppm) were observed, allowing a ready determination of the asymmetry induction by integration of the respective signals. Good to excellent selectivity was achieved for the two classes of ligands (dr from 80:20 to 96:04) using nonpolar solvent conditions (toluene-d_8 + 5% CD$_3$NO$_2$), the solvent having little influence over the diastereoselectivity. The ratios remained overall the same with the more polar CD$_2$Cl$_2$. These observations are summarized in Table 1, along with some spectroscopic information.

We have just described the synthesis and resolution of a novel chiral hexacoordinated phosphate that behaves as an enantiopure anionic N-ligand. This TRISPHAT-N anion, although binding at a single point, acts as an effective chiral auxiliary able to control with high selectivity the conformation of *tropos* ligands and the configuration of stereogenic metal ions. Further studies are being performed to exploit the asymmetric potential of anion **2** and the interesting chromatographic, air, and moisture stability that it confers to Lewis acidic metal complexes.

Supporting Information Available: CIF files giving crystal data for [**4**][Δ-**2**] and [Cu(*P*-**5a**)(Δ-**2**)], text giving spectroscopic data for the salts [^{n}Bu$_3$NH][*rac*-**2**], [**4**][Δ-**2**], [^{n}Bu$_4$N][Δ-**2**], and [^{n}-Bu$_4$N][Λ-**2**], and figures giving ^{1}H and ^{31}P NMR spectra of the aforementioned organometallic complexes. This material is available free of charge via the Internet at http://pubs.acs.org.

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(22) Brunner, H.; Klankermayer, J.; Zabel, M. *Organometallics* **2002**, *21*, 5746−5756.

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