Effective chiral recognition among ions in polar media†

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Effective homochiral recognition occurs between the cationic [Fe(eilatin)$_3$]$^{2+}$ complex and TRISPHAT anions even in polar media such as 90% acetone–CHCl$_3$ (de ≥ 89%).

Metal-directed and metal-templated syntheses allow nowadays the simple preparation of complexes of original structure and geometry.[1] In many instances, the derivatives are chiral and are obtained only as racemates due to the presence of an equilibrium between the enantiomers in solution. To obtain these compounds in one predominant configuration, stereogenic elements can be introduced in the backbone of the ligands;[2] one of the interconverting diastereomers is favored by intramolecular (inter-ligand) discriminating interactions.[3] Alternatively, if the complexes are charged, their configuration can be controlled *via* an association with chiral counter-ions;[4] intermolecular (interionic) diastereoselective interactions occur and induce stereoselectivity (*Pfeiffer* effect).[5]

In this context, enantiopure TRISPHAT anion (**1**, (tris(tetra-chlorobenzenediolato)phosphate(V), Δ or Λ enantiomers, Fig. 1),[6] has been shown to be a valuable asymmetry-inducing reagent for cationic metallo-organic complexes.[7] For instance, when associated with configurationally labile [Fe(4,4′-Me$_2$bpy)$_3$]$^{2+}$ **2** (bpy = 2,2′-bipyridine), two anions **1** control effectively the Δ or Λ configuration of the iron(II) complex.[8] A diastereomeric excess (de) higher than 96% was measured in CDCl$_3$ in favor of the homochiral salts [Δ-**2**][Δ-**1**]$_2$ or [Λ-**2**][Λ-**1**]$_2$.[8a,c]

While efficient chiral recognition is thus regularly achieved among ions in low polarity solvents, it is not the case in high polarity solvents as a result of weak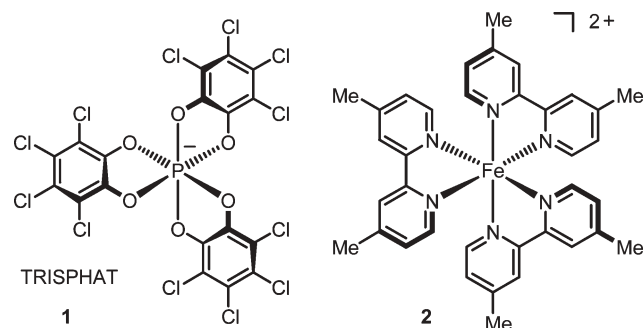er electrostatic interactions and solvent competition. Cations and anions behave as dissociated ion pairs and hence there is a sharp decrease in diastereoselectivity (*e.g.*, de 8% for salt [**2**][Δ-**1**]$_2$ in 50% DMSO-d_6–CDCl$_3$). It was thus debatable whether effective interionic chiral recognition could ever be achieved in polar solvent media. Herein we report the association of TRISPHAT anions with the iron(II) tris(diimine) complex of eilatin (**3**, Fig. 2) which leads to a remarkable level of stereoselective induction even in polar conditions (de > 89% in 90% acetone–chloroform).[9]

Eilatin (**3**) is a pyrido[2,3,4-*kl*]acridine marine alkaloid that was isolated from the Red Sea purple tunicate *Eudistoma sp.*[10] It can be viewed as a fused heptacyclic polypyridyl-type ligand that consists of a bpy-type "head" and a biq-type "tail" fused together back-to-back (see Fig. 2).[11] Recently, the utilization of eilatin as a ligand for Ru(II) and Os(II) complexes was reported.[12] These eilatin complexes exhibit a unique combination of properties that differentiate them from the vast array of Ru(II) and Os(II) polypyridyl complexes:[11,12] (a) preferential binding of the eilatin ligand through its less sterically hindered bpy-type "head"; (b) one of the most facile ligand-centered reductions and lowest energy ^{1}MLCT transitions ever observed, due to the low π* orbital of the highly delocalized eilatin ligand, leading to a distinct green color; (c) solution and solid-state aggregation by π-stacking interactions of the eilatin ligands.

Realizing that a D_3-symmetric tris(diimine) iron(II) complex of eilatin would offer (i) an open access to anions along the C_3-axis (Fig. 2), (ii) a strong hindrance along the C_2-axes, and (iii) planar rigid extensions at the 4,4′ positions of the "bpy" head, the association of such a complex with TRISPHAT anions was considered; all properties (i) to (iii) favor discriminating homo-chiral interactions between the three-bladed propellers.[13] Such a complex had never been reported before, so it was decided to attempt its preparation and its association with the chiral anions.[14] We postulated that effective chiral recognition between the ions might be strong enough to be maintained even in polar solvent media.
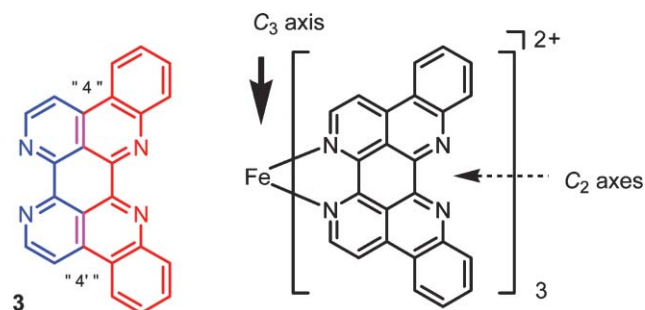

Fig. 1 TRISPHAT anion **1** and [Fe(Me$_2$bpy)$_3$]$^{2+}$ **2** (Δ enantiomers).

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Fig. 2 Eilatin **3** and schematic representation of its iron(II) complex **4**.

Tris(eilatin)iron(II) bis(TRISPHAT) salts, compounds [4][Δ-1]₂ and [4][Λ-1]₂, were prepared in a single step process. Treatment of FeCl₂·4H₂O with eilatin 3 (3.0 equiv.) in MeOH : water (2 : 1) at 20 °C (24 h) and extraction of the resulting solution with an appropriate source of TRISPHAT anion (2.0 equiv.)[15] afforded in the organic layer [CH₂Cl₂–acetone (9 : 1)] the desired green salts as the major products, [4][Δ-1]₂ (80%, [α]$_D$ = −4680) and [4][Λ-1]₂ (70%, [α]$_D$ = +4560).[16,17]

The chiral recognition was then studied by ¹H NMR spectroscopy.[18] Solutions of salt [4][Δ-1]₂ were prepared in acetone-d_6–CDCl₃ (0% to 90%, 5.4 × 10⁻⁴ M). In accordance with our expectations, a very high diastereomeric ratio was obtained. As a matter of fact, only one set of signals was visible for the coordination complex in all the different NMR spectra.[19] Even in 90% acetone-d_6–CDCl₃ conditions, a careful analysis revealed the presence of a single diastereomeric species; lower signal : noise ratio in this solvent mixture allowed us, however, only to estimate a higher than 90% diastereoselectivity (see supporting information†).[20]

To verify that the choice of acetone and chloroform mixtures as solvent was not particular, complex [2][Δ-1]₂ was studied under similar conditions. In this case, distinguishable signals were observed for the diastereomeric homochiral [Δ-2][Δ-1]₂ and heterochiral [Λ-2][Δ-1]₂ salts in solutions containing 10% or more of acetone. The diastereoselectivity of the induction could thus be measured by the integration of the respective signals (Table 1, supporting information†).[21] As previously observed, complete chiral recognition was achieved only in CDCl₃.[8a] Upon increasing the solvent polarity (higher percentage acetone-d_6), a gradual decrease in diastereoselectivity was observed that reached a low value of 20% de in 90% acetone-d_6–CDCl₃. These results and those of the eilatin complex are summarized in Table 1. They clearly indicate that better chiral recognition is achieved with eilatin complex 4 in comparison to Me₂bpy complex 2.

The ion pairing was then studied by circular dichroism (CD) to establish the homochiral or heterochiral nature of the salt and the efficiency of the chiral recognition at lower concentrations (∼10⁻⁵ M range). The initial results were somewhat puzzling as the CD spectra of solutions of complex [4][Δ-1]₂ revealed positive and negative Cotton effects around 632 and 718 nm respectively (see Fig. 3), whereas complex [2][Δ-1]₂ displayed, as expected,[22] negative and positive Cotton effects around 488 and 558 nm respectively (CHCl₃, 2 × 10⁻⁵ M, supporting information†).

Fig. 3 UV and induced CD spectra of salts (a) [4][Δ-1]₂ (red) and (b) [4][Λ-1]₂ (blue), chloroform, 2 × 10⁻⁵ M, 20 °C.

Rather than attribute the sign reversal of the Cotton effects at the lowest energies to a heterochiral association for salt [4][Δ-1]₂, we reasoned that the type of transition pertaining to the bands was different in complexes 2 and 4.[23] To establish the nature of the ion pairing, a more "classical" analysis of the π–π* transitions of salts [2][Δ-1]₂ and [4][Δ-1]₂ was thus performed. It was necessary to subtract the contribution of TRISPHAT anion Δ-1, which is CD-active in the 240–340 nm region.[24] The resulting CD spectra then subsequently matched our expectations as both salts presented positive and negative bands for the exciton couplet at lower and higher wavelengths respectively (2: Δε₂₈₇ = +63 and Δε₃₀₃ = −148 M⁻¹ cm⁻¹; 4: Δε₂₅₂ = +80 and Δε₂₇₆ = −141 M⁻¹ cm⁻¹, CH₂Cl₂, 2 × 10⁻⁶ M). This result is in complete agreement with a Δ configuration for both complexes 2 and 4 (Fig. 4).

The homochiral nature of the ion pairing being ascertained, the efficiency of the chiral recognition at lower concentration was studied. Diluted solutions of [Δ-2][Δ-1]₂ and [Δ-4][Δ-1]₂ were prepared in acetone–CHCl₃ (0% to 90%, 4 × 10⁻⁵ M) and their CD spectra recorded. As expected, a variation of the Cotton effects was noticed upon changes in solvent polarity (see supporting information†). Assuming that the diastereoselectivity remains quasi perfect in chloroform, a quantitative analysis of the CD spectra was performed using 99 and 98% values for the diastereoselectivity within salts [4][Δ-1]₂ and [2][Δ-1]₂ respectively. The results are summarized in Table 1. For compound [4][Δ-1]₂, values in good agreement with those of the NMR experiments were obtained. For complex [2][Δ-1]₂, the analysis of the 488 or 558 nm bands gives similar results. In this case, better chiral

Table 1 Diastereoselectivity (de) of the chiral recognition between anions 1 and cationic complexes 2 and 4

| Acetone[a] | [4][Δ-1]₂ | | [2][Δ-1]₂ | | |
	de NMR[b]	de CD[c,d]	de NMR[e]	de CD[c,f]	de CD[c,g]
0%	>98%	99%[h]	>98%	98%[g]	98%[h]
10%	>98%	98%	76%	90%	91%
20%	>98%	98%	72%	76%	78%
50%	>98%	98%	50%	24%	27%
90%	>90%[i]	89%	20%	3%	3%

[a] In CHCl₃. [b] 5.4 × 10⁻⁴ M. [c] 4 × 10⁻⁵ M. [d] From the Cotton effect measured at 635 nm. [e] 6.7 × 10⁻⁴ M. [f] From the Cotton effect measured at 488 nm. [g] From the Cotton effect measured at 558 nm. [h] Estimated. [i] Some precipitation was observed in this solvent condition.
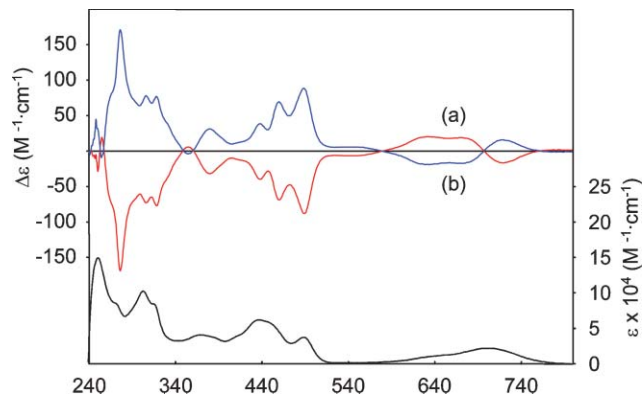

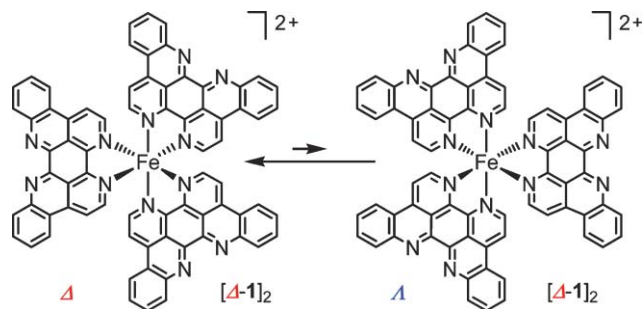**Fig. 4** Preferred homochiral ion pairing of 4 and anions Δ-1.

recognition seems to be achieved in low polarity conditions ($\leqslant 20\%$ acetone) with, however, a sharper decrease in diastereoselectivity with a higher content of acetone.

In conclusion, experimental data indicate that the diastereo-selective induction from TRISPHAT anions onto the tris(eilatin)iron(II) complex occurs with unprecedented high selectivity even in polar media.

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14 Analysis of [**4**][PF$_6$]$_2$ prepared independently supported a mononuclear D_3 symmetric Fe(eilatin)$_3$]$^{2+}$ complex in which the eilatin ligand was bound *via* its "head": ^{1}H NMR ((CD$_3$)$_2$SO, 500 MHz): δ 8.93 (d, $J = 7.8$ Hz, 1H, H^c), 8.86 (d, $J = 6.1$ Hz, 1H, H^b), 8.62 (d, $J = 8.1$ Hz, 1H, H^f), 8.16 (t, $J = 8.0$ Hz, 1H, H^e), 8.00 (m, 2H, H^d, H^a); ^{13}C NMR: δ 153.3 (C–H^a), 134.3 (C–H^e), 132.9 (C–H^f), 131.4 (C–H^d), 125.5 (C–H^c), 123.3 (C–H^b); FABMS, 1125 [M – 2PF$_6$]$^+$. See ref. 11 for eilatin proton assignment.

15 Salts [Bu$_3$NH$^+$][Λ-**1**] (>96% ee) or [cinchonidinium][Δ-**1**] (100% de) were used. See ref. 6*b*.

16 Measured in CHCl$_3$ ($c = 0.0054$, 20 °C).

17 No traces of **3** can be seen in the NMR spectra taken immediately after the dissolution of complexes [**4**][**1**]$_2$. Eilatin appears slowly in solution with a maximum percentage of 6–7%.

18 This study has been performed with anion Δ-**1** only. Previous work (ref. 8*a*) with both Δ-**1** or Λ-**1** has shown no difference between the enantiomeric systems, except chiroptical ones obviously.

19 Only trace amount of the eilatin ligand can be seen along with the signal of one diastereomeric complex. See ref. 17.

20 In 90% acetone-d_6–CDCl$_3$, salt [Fe(**3**)$_3$](Δ-**1**)$_2$ is poorly soluble and precipitation of both complex and ligand is observed.

21 T1 relaxation times differ for the protons of the diastereomeric salts (*e.g.*, 430 and 740 ms for H4 of Λ-**2** and Δ-**2** respectively). A delay of 5 s between scans was chosen to allow a clean integration.

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