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Supramolecular Stereocontrol of Octahedral Metal-Centered Chirality. Ligand Modulation

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By associating chiral labile $[FeL_3]^{2+}$ complexes with TRISPHAT anions, a stereocontrol of the metal-centered chirality is feasible; the sense of the stereoselective induction and its magnitude strongly depends upon the structure of the diimine ligands (L: bpy, phen).

Much progress has been made in metal-directed and metal-templated synthesis to allow chemists to prepare molecular and supramolecular complexes of original structure and geometry.[1] In many instances, the derivatives are chiral and are obtained only as racemates due to the presence in solution of an equilibrium between the enantiomers. To obtain these compounds in one predominant configuration, a possible strategy is to introduce stereogenic elements to the backbone of the ligands;[2] intramolecular discriminating interactions happen and favor one of the interconverting diastereomers.[3] If the complexes are charged, a complementary strategy to control their configuration is to consider their ion pairing with chiral counterions;[4] intermolecular diastereoselective interactions can induce a stereoselective induction (Pfeiffer effect).[5]

Recently, chiral TRISPHAT anion **1** (tris(tetrachlorobenzenediolato)phosphate(v), Λ or Δ enantiomers, Figure 1)[6] has been shown to be a valuable resolving and asymmetry-inducing reagent for cationic metalloorganic and organometallic complexes.[7] For instance, associated with configurationally labile $[Fe(phen)_3]^{2+}$ **2** and $[Fe(4,4'\text{-}Me_2bpy)_3]^{2+}$ **6**, two anions **1** control effectively the Δ or Λ configuration of the iron(II) complexes (phen = 1,10-phenanthroline; bpy = 2,2′-bipyridine).[8] Diastereomeric ratios higher than 49:1 were measured in $CDCl_3$ in favor of the homochiral salts.[8a,c] The characterization and quantification of the asymmetry induction was performed by circular dichroism (CD) and by NMR spectroscopy as the anions are, in addition, good chiral shift agents.[7]

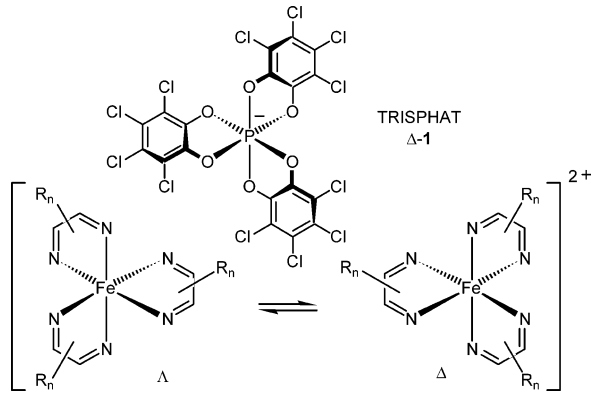

Figure 1. Interconversion between Λ and Δ enantiomers of $[Fe(diimine)_3]^{2+}$ complexes and possible stereoselective induction from enantiopure TRISPHAT anion **1**.

This supramolecular approach to the stereocontrol of octahedral metal centers allows a simple access to both

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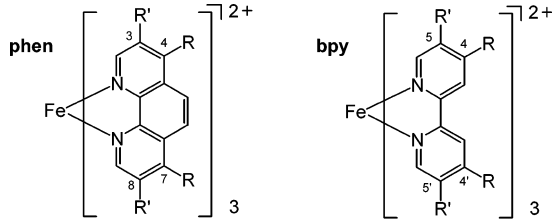

R = H R' = H **2**
R = Me R' = H **3**
R = H R' = Me **4**

R = H R' = H **5**
R = Me R' = H **6**
R = Et R' = H **7**
R = Bn R' = H **8**
R = ^{i}Pr R' = H **9**
R = ^{t}Bu R' = H **10**
R = H R' = Me **11**

Figure 2. Iron(II) complexes **2** to **11**.

configurations of a chiral cation by exchange, at the end of the synthesis, of traditional anions (PF_6^-, BF_4^-, etc.) by TRISPHAT counterions. This can render the stereoselective synthesis of coordination complexes very simple. However, chiral tris(diimine) metal complexes adopt a variety of shapes due to the many different ligands that can be brought into the first coordination sphere. It was thus debatable whether anion **1** is generally effective as a chiral noncovalent auxiliary. This prompted us to investigate its chiral recognition with a rather large family of complexes. Herein, we report that the diastereoselectivity and the homochiral or heterochiral nature of the induction strongly depend upon the nature of the ligands.

The goal was thus to associate TRISPHAT anions **1** with a large variety of complexes (**2** to **11**, Figure 2) made from structurally different ligands. Care was taken to choose diimine moieties made of bpy and phen backbones as the differences in the skeletons (flexible/rigid, planar/nonplanar) could influence the selectivity. Size, shape, and position of substituents on the ligands were also foreseen to be factors that could influence the chiral recognition and therefore the diastereoselectivity. Alkyl groups were thus introduced at the 4,4′- and 5,5′-positions of bpy ligands as well as at the analogous 4,7- and 3,8-positions of phen derivatives. The derived tris(diimine)iron(II) bis(TRISPHAT) salts, compounds (**2**)(Δ-**1**)$_2$ to (**11**)(Δ-**1**)$_2$, were prepared according to reported conditions.[8]

The diastereoselectivity of the ion pairing of cations **2**−**11** with anions Δ-**1** was first studied by ^{1}H NMR spectroscopy.[9] Solutions of salts (**2**)(Δ-**1**)$_2$ to (**11**)(Δ-**1**)$_2$ were prepared in DMSO-d_6/$CDCl_3$ (0% to 20%, 1.0 mM), and their NMR spectra showed partial or complete enantiodifferentiation of the cation. Distinguishable signals for the diastereomeric homochiral [Δ-(**2**−**11**)](Δ-**1**)$_2$ and heterochiral [Λ-(**2**−**11**)]-(Δ-**1**)$_2$ salts were always observed, and the diastereoselectivity of the induction could thus be measured by the integration of the respective signals (Table 1, Supporting Information).[10] As previously observed, upon decreasing solvent polarity (lower % DMSO), one diastereomer of complexes (**2**−**11**)(Δ-**1**)$_2$ becomes predominant (with the exception of **9**). The increase in diastereoselectivity as the polarity decreases is interpreted as the result of closer interactions between the ions.[11] In Figure 3 are detailed some of the ^{1}H NMR spectra of salt (**3**)(Δ-**1**)$_2$ made from 4,7-Me_2phen. In this case, the chiral recognition is particularly efficient as a diastereoselectivity ratio of 49:1 is obtained in rather polar medium (12.5% DMSO-d_6/$CDCl_3$).

Table 1. Stereoselective Induction of Anions Δ-**1** onto Complexes **2** to **11** as a Function of Solvent Polarity[a]

	complex									
% DMSO[b]	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**
0	>97	>97	93	*c*	>97	89	44	0	−59	*c*
2.5	97	97	85	*c*	95	77	37	3	−47	−29
5	95	97	75	*c*	92	69	28	6	−33	−13
7.5	91	97	65	51	87	56	24	6	−24	−4
10	82	97	57	43	80	51	*d*	7	−16	−1
12.5	73	97	48	35	73	44	19	6	*d*	−1
15	66	95	41	28	66	34	15	7	−6	0
20	45	79	24	19	47	19	6	7	0	2

[a] Diastereomeric excess (de, %). Positive and negative values represent homochiral and heterochiral association, respectively. [b] % DMSO in $CDCl_3$. [c] Precipitation of the salt. [d] Not measurable due to overlaps.

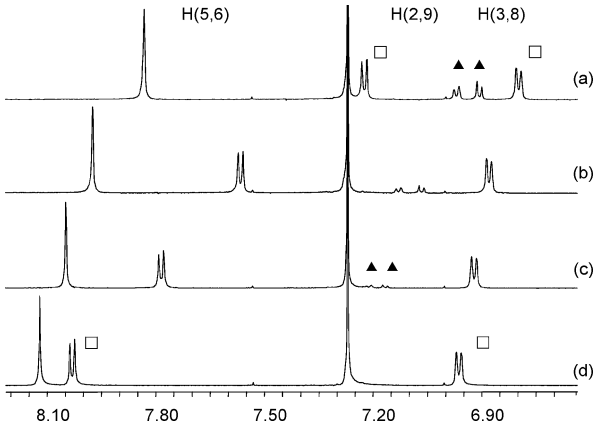

Figure 3. Diastereoselective interaction of **3** and anions Δ-**1**. ^{1}H NMR (400 MHz) in DMSO-d_6/$CDCl_3$: (a) 30%, de 48%; (b) 20%, de 79%; (c) 15%, de 95%; (d) 10%, de >97%. Signals of aromatic protons of homochiral (□) and heterochiral (▲) salts.

CD spectra of solutions of complexes (**2**−**9**)(Δ-**1**)$_2$ (0.1% DMSO in $CHCl_3$) revealed negative and positive Cotton effects around 480 and 560 nm, respectively. Both the CD and electronic spectra of **1** are transparent in this region. These spectra can thus be assigned to a Δ configuration of the cationic complexes, demonstrating that compounds [Δ-(**2**−**9**)](Δ-**1**)$_2$ are the major diastereomers.[12] Some selected spectra are shown in Figure 4. However, the CD spectra of (**10**−**11**)(Δ-**1**)$_2$ revealed an opposite situation. In these latter cases, a preferred Λ configuration of the cations is clearly shown. The asymmetric induction from the TRISPHAT anions can thus happen with either a homochiral

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

(10) T_1 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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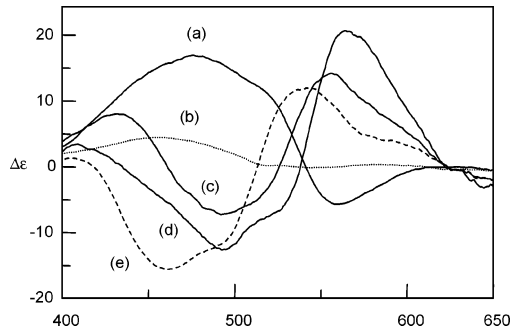

Figure 4. Selected CD spectra in the region of the MLCT bands (λ 400−650 nm): (a) (**10**)(Δ-**1**)$_2$; (b) (**11**)(Δ-**1**)$_2$; (c) (**3**)(Δ-**1**)$_2$; (d) (**6**)(Δ-**1**)$_2$; (e) (**4**)(Δ-**1**)$_2$.

or a heterochiral relationship depending upon the ligands coordinated to the iron atom (Table 1).

Several trends can be extrapolated from the spectroscopic data. A gradual increase in the bulk of substituents at the 4,4′-positions (from Me to ^{i}Pr) of bpy ligands results in a gradual decrease in the diastereoselectivity of the homochiral induction (**6** to **9**). With ^{i}Pr substituents (**9**), an induction is practically not observed both in CD and in NMR spectroscopy. A final increase in the size of the 4,4′-residues (^{t}Bu groups) leads then to the heterochiral selectivity (Figure 4). The diastereoselectivity (de −59% in $CHCl_3$) in favor of the (Λ-**11**)(Δ-**1**)$_2$ complex remains however modest.[13] Changing the position of methyl substituents from 4,4′- to 5,5′-positions also results in a loss and a reversal of selectivity (**11** vs **6**).

Contrary to bpy derivatives, all phen complexes (**2**−**4**) lead to a high homochiral asymmetric induction in $CHCl_3$ (de > 93%, Table 1). Direct comparison of related systems, i.e., **2** and **5** (R,R′ = H), **3** and **6** (R = Me), **4** and **11** (R′ = Me), reveals that much better selectivity occurs with phen derivatives. This might be due to the rigidity of these ligands, which allows a beneficial preorganization of the iron(II) complexes for the chiral recognition.[14] Orientation of methyl substituents along the C_3 axis (**4** vs **3**) leads to a lower selectivity, although without a reversal of the sense of induction.

A preliminary explanation for some of these effects can be drawn from the NMR comparison of salts (**6**)(Δ-**1**)$_2$ and (**6**)$(PF_6)_2$. Solutions of (**6**)$(PF_6)_2$ were prepared in mixtures of DMSO-d_6 (0 to 90%)/$CDCl_3$, and the difference in the chemical shifts ($\Delta\delta$) between the protons of diastereomeric salts (Δ-**6**)(Δ-**1**)$_2$, (Λ-**6**)(Δ-**1**)$_2$, and (**6**)$(PF_6)_2$ was calculated. In 90% DMSO-d_6/$CDCl_3$, identical chemical shifts ($\Delta\delta$ = 0) are observed for all salts. The cation and anions behave as dissociated ion triples in such a polar medium. However, upon decreasing the solvent's polarity, a gradual increase in $\Delta\delta$ values is observed. Anions Δ-**1** have clearly a larger influence on the predominant homochiral salt than on the minor hetereochiral salt (Table 2, Supporting Information). For (Δ-**6**)(Δ-**1**)$_2$, the most shifted signals correspond to protons H_6, which are shifted at higher frequency, compared to the reference, whereas all other ones move upfield. Signals become less perturbed (lower $|\Delta\delta|$ value) when moving away from the C_3 axis in the direction of the C_2 axes: from protons H_6 to protons H_3. For (Λ-**6**)(Δ-**1**)$_2$, the situation is opposite with the methyl and H_3 protons being the most perturbed or shifted downfield, respectively.

Table 2. Chemical Shifts (δ) and Difference in Chemical Shifts ($\Delta\delta$) for the Protons of (Δ-**6**)(Δ-**1**)$_2$ and (Λ-**6**)(Δ-**1**)$_2$ Salts Compared to (**6**)$(PF_6)_2$ (^{1}H NMR, 400 MHz, 5% DMSO-d_6/$CDCl_3$)

	$\delta_{\Delta\Delta}$[a]	$\delta_{\Delta\Lambda}$[b]	δ_{ref}[c]	$\Delta\delta_{(\Delta\Delta-ref)}$	$\Delta\delta_{(\Delta\Lambda-ref)}$
H_6	7.469	6.928	6.964	0.647	−0.072
H_5	6.806	7.034	7.059	−0.309	−0.055
H_{Me}	2.180	2.343	2.414	−0.308	−0.116
H_3	8.117	8.211	8.175	−0.075	0.068

[a] (Δ-**6**)(Δ-**1**)$_2$. [b] (Λ-**6**)(Δ-**1**)$_2$. [c] Reference salt (**6**)$(PF_6)_2$.

The result of this experiment is in agreement with a preferred association of ions Δ-**1** along the C_3 axis and C_2 axes of cation **6** in the homochiral and heterochiral salts, respectively.[15] It explains why the steric hindrance along the C_3 axis created by the 5,5′-methyl groups of the bpy ligands in complex **11** disfavors the homochiral salt (Δ-**11**)(Δ-**1**)$_2$. It also explains why, on the contrary, a homochiral association is preferred with phen complexes **2**−**4**, the presence of the "extra" medium ring obstructing strongly the approach of the enantiopure anion along the C_2 axes disfavoring the heterochiral association.

In conclusion, experimental data indicate that the diastereoselective induction from TRISPHAT anions onto tris(diimine)iron(II) complexes occurs with better selectivity with phen rather than bpy ligands. The homochiral vs heterochiral nature of the induction, as well as its diastereoselectivity, strongly depends upon the backbone and the size and position of substituents. Studies are conducted to investigate further the nature of the ion pairing.

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Supporting Information Available: NMR spectra of salts (**2**)(Δ-**1**)$_2$ to (**11**)(Δ-**1**)$_2$ in DMSO-d_6/$CDCl_3$ (20% to 0%). Selected CD spectra in the UV region. Diagram of the difference in chemical shifts ($\Delta\delta$) for the protons of (Δ-**6**)(Δ-**1**)$_2$ and (Λ-**6**)(Δ-**1**)$_2$ salts compared to those of (**6**)$(PF_6)_2$. This material is available free of charge via the Internet at http://pubs.acs.org.

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(13) Positive and negative values represent homochiral and heterochiral association, respectively.

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