

# Ion pair chromatographic resolution of tris(diimine)ruthenium(II) complexes using TRISPHAT anions as resolving agents

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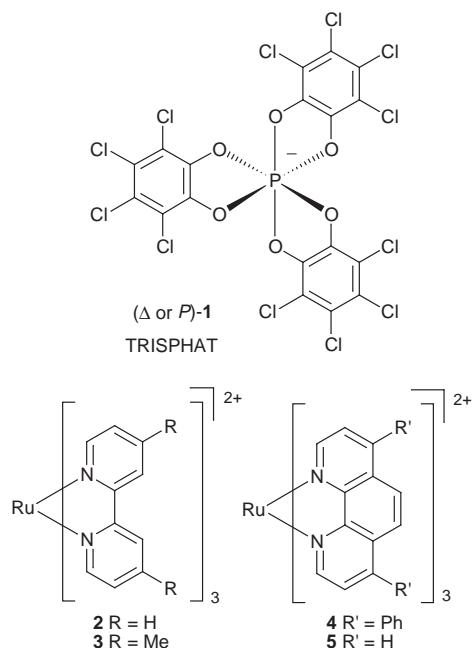
**Enantiomers of chiral tris(diimine)ruthenium(II) complexes can be separated on a polar chromatographic phase (SiO<sub>2</sub>) when associated with TRISPHAT counterions (2 equivalents).**

Chiral tris(diimine)ruthenium(II) complexes have been extensively studied in the fields of photochemistry and photo-physics, and as probes in DNA.<sup>1</sup> Many applications require enantiopure complexes ( $\Delta$  or  $\Lambda$ ) and, for those made from achiral ligands, a resolution is usually needed due to the shortage of enantioselective methods of synthesis.<sup>2</sup> Traditionally, resolutions of chiral cationic tris(diimine)ruthenium(II) complexes are realised by the formation of diastereomeric ion pairs (IPs) with anionic chiral resolving agents, and then depend principally on solubility differences.<sup>3</sup> Ion-pair chromatographic resolutions, using cation exchangers and electrolytes with chiral anions in the mobile phase, are possible and lead to efficient separation of diastereomeric IPs.<sup>4</sup> Herein, we report a new chromatographic resolution procedure involving pre-formed diastereomeric mixtures of chiral tris(diimine)ruthenium(II) complexes and TRISPHAT anions (**1**, 2 equiv.). The resulting

profoundly the chromatographic properties of cations associated with it (e.g. triarylcarbenium cations) and the resulting IPs are poorly retained on polar chromatographic phases.<sup>6b</sup> This result encouraged us to examine whether enantiopure TRISPHAT anion could be used for the IP chromatographic resolution of configurationally stable chiral cations, such as the tris(diimine)ruthenium(II) complexes. We hypothesised that selective chiral discriminating interactions would occur between these three-bladed propellers ( $\Delta^+-\Delta^-$  vs.  $\Lambda^+-\Delta^-$ ) resulting in a good separation.<sup>6c</sup> We decided to test this hypothesis with [Ru(bipy)<sub>3</sub>]<sup>2+</sup> **2**, [Ru(4,4'-diMebipy)<sub>3</sub>]<sup>2+</sup> **3**, [Ru(bathophen)<sub>3</sub>]<sup>2+</sup> **4** and [Ru(phen)<sub>3</sub>]<sup>2+</sup> **5** complexes using the cinchonidinium-(*P* or  $\Delta$ )-**1** salt (**1a**) as resolving agent.<sup>5,6a</sup> Complexes **2-Cl**<sub>2</sub> and **3-Cl**<sub>2</sub> were prepared following the description of Broomhead and Young,<sup>7</sup> and salts **3-(PF<sub>6</sub>)<sub>2</sub>**, **4-(PF<sub>6</sub>)<sub>2</sub>** and **5-(PF<sub>6</sub>)<sub>2</sub>** in a single step from Ru(DMSO)<sub>4</sub>Cl<sub>2</sub> and the respective bipyridine or phenanthroline ligands (3 equiv.).<sup>8</sup>

The potential of TRISPHAT **1** to serve as a chromatographic resolving agent was first evaluated by analytical thin layer chromatography (TLC): Solutions of salt **1a** (2.0 equiv.) in acetone and racemic **2-Cl**<sub>2</sub>, **3-Cl**<sub>2</sub>, **3-(PF<sub>6</sub>)<sub>2</sub>** or **4-(PF<sub>6</sub>)<sub>2</sub>** (1.0 equiv.) in CH<sub>2</sub>Cl<sub>2</sub> were prepared, mixed together, and the resulting solutions adsorbed on silica gel plates. Development by elution with CH<sub>2</sub>Cl<sub>2</sub> or CHCl<sub>3</sub> showed the formation of two bands corresponding to the two new diastereomeric IPs, [ $\Delta$ -(**2-4**)]( $\Delta$ -**1**)<sub>2</sub> and [ $\Lambda$ -(**2-4**)]( $\Delta$ -**1**)<sub>2</sub>. Much reduced affinity for silica gel was exhibited as foreseen, as the (**2-4**)( $\Delta$ -**1**)<sub>2</sub> IPs were retained to a much lower extent (Table 1).

The retention of diastereomeric salts (**2-4**)( $\Delta$ -**1**)<sub>2</sub> depended upon the nature of the cation and the concentration of the salts.<sup>6b</sup> Solutions were thus applied (spotted) as concentrated as possible. Due to the streaking of salts (**2-4**)( $\Delta$ -**1**)<sub>2</sub> on TLC, we have not calculated retardation factors (*R<sub>f</sub>*), but rather measured the distance moved by the analyte band to the top (and not to the centre) of the spot: The derived ratios, called just *R*, for the resulting IPs were in the range of 0.45–0.75 for the most eluted diastereomer and 0.35–0.54 for the least (CH<sub>2</sub>Cl<sub>2</sub> as eluent). We observed rather large differences between the *R* values of the diastereomeric IPs (max.  $\Delta R = 0.23$ ). More lipophilic cations (**3** and **4**, entries 2–5) were retained less than **2** and **5**. The less polar CHCl<sub>3</sub> led to better separation than CH<sub>2</sub>Cl<sub>2</sub>. The nature of



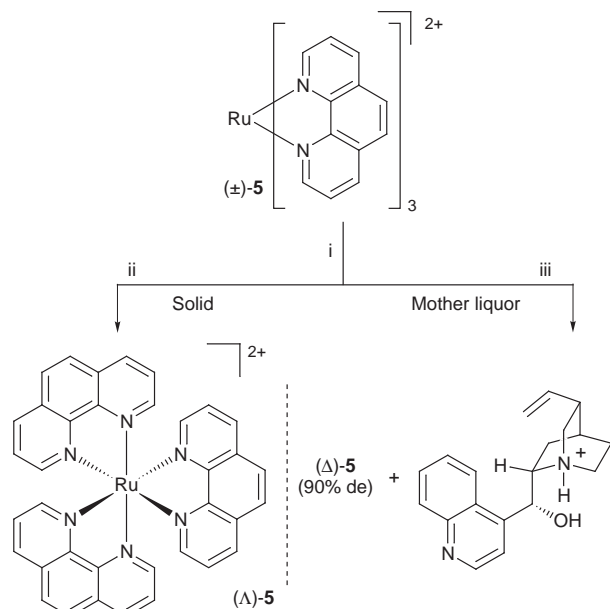
diastereomeric IPs are poorly retained on polar chromatographic phase (SiO<sub>2</sub>) and large differences in the retardation factors are observed.

Recently, we have shown that the easily prepared and resolved chiral TRISPHAT anion **1** [tris(tetrachlorobenzene-diolato)phosphate(v)] is configurationally stable as an ammonium salt in solution.<sup>5</sup> Anion **1** is an efficient NMR chiral shift agent and a valuable host in molecular recognition studies, conferring unique properties to its IPs.<sup>6</sup> For instance, TRISPHAT modifies

**Table 1** Retardation factors of diastereomeric [Ru(LL)<sub>3</sub>]( $\Delta$ -**1**)<sub>2</sub>

Entry	Racemic salt	<i>R</i> <sup>a,b</sup> ( <b>2-5</b> )-X <sub>2</sub>	<i>R</i> ( <b>2-5</b> )( $\Delta$ - <b>1</b> ) <sub>2</sub> <sup>a,b</sup>		
			Most eluted	Least eluted	$\Delta R$
1 <sup>c</sup>	<b>2</b> (Cl) <sub>2</sub>	< 0.05	0.45	0.33	0.12
2 <sup>c</sup>	<b>3</b> (Cl) <sub>2</sub>	< 0.05	0.75	0.52	0.23
3 <sup>c</sup>	<b>3</b> (PF <sub>6</sub> ) <sub>2</sub>	< 0.05	0.76	0.54	0.22
4 <sup>c</sup>	<b>4</b> (PF <sub>6</sub> ) <sub>2</sub>	0.08	0.75	0.65	0.10
5 <sup>d</sup>	<b>4</b> (PF <sub>6</sub> ) <sub>2</sub>	0.15	0.65	0.46	0.19
6 <sup>c</sup>	<b>5</b> (PF <sub>6</sub> ) <sub>2</sub> <sup>e</sup>	< 0.05	0.42	<i>f</i>	<i>f</i>

<sup>a</sup> *R* represents the distance moved by the analyte band to the top. <sup>b</sup> Spotted as concentrated as possible. <sup>c</sup> CH<sub>2</sub>Cl<sub>2</sub> as eluent. <sup>d</sup> CHCl<sub>3</sub> as eluent. <sup>e</sup> TLC done with solution containing partially resolved  $\Delta$ -**5**. <sup>f</sup> Not applicable.



**Scheme 1** Reagents and conditions: i, 1.0 equiv. of  $(\pm)$ -**5**-(PF<sub>6</sub>)<sub>2</sub> in CH<sub>2</sub>Cl<sub>2</sub>, 2.0 equiv. of **1a** in acetone, CH<sub>2</sub>Cl<sub>2</sub>, 10 min; ii, filtration, essentially  $\Delta$ -**5**; iii, mother liquor, cinchonidinium: $\Delta$ -**5** (4:1), de 90%

the anionic counterion (Cl<sup>-</sup>, PF<sub>6</sub><sup>-</sup>) in the precursor salt seems to have, within experimental error, no influence (entries 2 and 3). The behaviour of the (2-4)( $\Delta$ -**1**)<sub>2</sub> ion pairs is quite remarkable as the precursor salts (2-4)(PF<sub>6</sub>)<sub>2</sub> migrate little under these chromatographic conditions.

TLC analysis of racemic salt **5**-(PF<sub>6</sub>)<sub>2</sub> in the presence of anions  $\Delta$ -**1** could not be completed as planned: The precipitation of an orange solid containing essentially  $\Delta$ -**5** was observed in seconds upon the mixing of the solutions of **5**-(PF<sub>6</sub>)<sub>2</sub> and **1a**.<sup>‡</sup> A direct, yet partial, resolution of **5** was thus afforded as the filtration of the solid gave a mother liquor containing the cinchonidinium cation and  $\Delta$ -**5** (90% de) in a 4:1 ratio (Scheme 1).

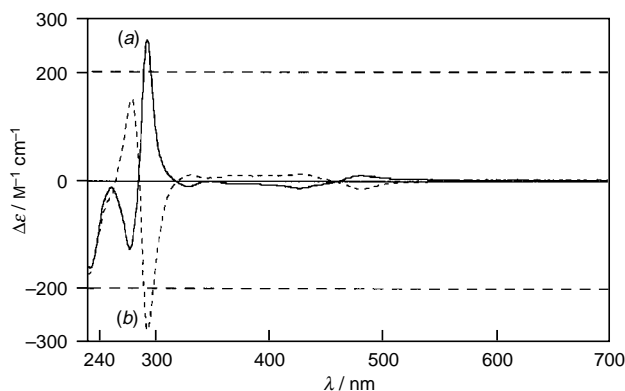
Preparative chromatographic resolution was possible for the ruthenium(II) diimine complexes **3** and **4**, exhibiting good solubility in CH<sub>2</sub>Cl<sub>2</sub> (or CHCl<sub>3</sub>) and large  $\Delta R$  values when associated with **1**. From mixtures of **1a** (2.0 equiv.) and racemic salts **3**-(PF<sub>6</sub>)<sub>2</sub> and **4**-(PF<sub>6</sub>)<sub>2</sub> (1.0 equiv.), pure separated diastereomeric IPs [ $\Delta$ -(**3,4**)]( $\Delta$ -**1**)<sub>2</sub> and [ $\Lambda$ -(**3,4**)]( $\Delta$ -**1**)<sub>2</sub> could be afforded in reasonable yields (Table 2):§

**Table 2** Preparative ion pair chromatographic resolution

Entry	Salts	Most eluted <sup>a</sup>	Least eluted <sup>a</sup>	Mixed fraction <sup>a</sup>	Eluents <sup>b</sup>
1	<b>3</b> -(PF <sub>6</sub> ) <sub>2</sub>	34% <sup>c</sup>	15% <sup>d</sup>	41%	A only
2	<b>3</b> -(PF <sub>6</sub> ) <sub>2</sub>	40% <sup>c</sup>	—	56% <sup>e</sup>	B then A
3	<b>4</b> -(PF <sub>6</sub> ) <sub>2</sub>	45% <sup>c</sup>	29% <sup>d</sup>	24%	B then A

<sup>a</sup> Yields for isolated products. <sup>b</sup> A = CH<sub>2</sub>Cl<sub>2</sub> and B = CHCl<sub>3</sub>. <sup>c</sup> Homochiral complex  $\Delta^+(\Delta^-)$ <sub>2</sub>. <sup>d</sup> Heterochiral complex  $\Lambda^+(\Delta^-)$ <sub>2</sub>. <sup>e</sup> The lower solubility of ( $\Delta$ -**3**)( $\Delta$ -**1**)<sub>2</sub> in CHCl<sub>3</sub> leads to its gradual release in solution and thus to an important contamination of the least eluted fraction.

The enantiomeric excesses of the cations in the various chromatographic fractions were easily assessed by TLC and/or determined precisely by <sup>1</sup>H NMR analysis.¶ Due to the streaking of the IPs on silica gel, the most rapidly eluted diastereomers were always afforded in better yields than the least, and rather large fractions containing both diastereomers were isolated. Circular dichroism (CD) analyses of solutions of the most and least rapidly eluted separated diastereomers indicated that the cationic complexes had absolute  $\Delta$  and  $\Lambda$  configurations respectively (Fig. 1). Homochiral [ $\Delta$ -(**3,4**)]( $\Delta$ -



**Fig. 1** CD spectra of the most and least eluted diastereomeric complexes (a) ( $\Delta$ -**3**)( $\Delta$ -**1**)<sub>2</sub> and (b) ( $\Lambda$ -**3**)( $\Delta$ -**1**)<sub>2</sub> in CH<sub>2</sub>Cl<sub>2</sub> at 20 °C

**1**)<sub>2</sub> complexes were less well retained than heterochiral complexes [ $\Lambda$ -(**3,4**)]( $\Delta$ -**1**)<sub>2</sub> on silica gel.

In conclusion, we have developed a new chromatographic resolution procedure for rather lipophilic cationic tris(diimine)ruthenium(II) complexes; it requires just 2 equiv. of the resolving agent and a polar chromatographic phase (SiO<sub>2</sub>), which thus makes it economical and practical.

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## Notes and References

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‡ <sup>31</sup>P NMR analyses (20% [<sup>2</sup>H<sub>6</sub>]DMSO-CDCl<sub>3</sub>) of the solid and the mother liquor reveal the presence of TRISPHAT and PF<sub>6</sub><sup>-</sup> in both fractions.

§ *Typical procedure*: To a solution of 67.7 mg of **3**-(PF<sub>6</sub>)<sub>2</sub> (71.7 μmol, 1.0 equiv.) in CH<sub>2</sub>Cl<sub>2</sub> (10 ml) was added a solution of 152.7 mg of **1a** (143.5 μmol, 2.0 equiv.) in acetone (5 ml) and, after 10 min of stirring, 1.0 g of SiO<sub>2</sub> [J. T. Baker silica gel (30–60 μm)]. The resulting mixture was concentrated *in vacuo* affording a fine orange powder, which was placed on the top of a chromatography column (SiO<sub>2</sub>, 3 × 18 cm). Elution with CH<sub>2</sub>Cl<sub>2</sub> afforded fractions that were collected, analysed by TLC/NMR and gathered according to their enantiomeric purity.

¶ The associated TRISPHAT anions behave as NMR chiral shift agents.

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