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Communication

# TRISPHAT salts. Efficient NMR chiral shift and resolving agents for substituted cyclometallated ruthenium bis(diimine) complexes

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Dedicated to Prof. Jean-François Normant

## Abstract

The determination of the enantiomeric purity of monocationic ruthenium(II) cyclometallated complexes is easily carried out by $^1$H-NMR analysis using a TRISPHAT salt as a diamagnetic chiral shift reagent. Resolution of the organometallic complexes can be conveniently carried by preparative thin layer chromatography using TRISPHAT as a chiral counter-ion. © 2001 Elsevier Science B.V. All rights reserved.

*Keywords:* Resolution; NMR enantiomeric purity determination; Ion pairing

## 1. Introduction

Recently, the synthesis and characterisation of cyclometallated bis(diimine)ruthenium(II) complexes has been studied due to the potential of these derivatives (**1**–**4**) to serve as cationic templates in crystal engineering studies and as "building blocks" for the constitution of molecular wires (Fig. 1). The remarkable kinetic stability of complex **1** [1] renders its functionalisation by electrophilic aromatic substitution possible — despite the presence of a formally carbanionic centre — and hence a large range of molecular architectures can be obtained by conventional organic chemistry [2]. Compound **2** — derived from **1** by reaction with NBS — reacts with methyl-2-butyn-3-ol-2 under Castro–Stephens–Sonogashira reaction conditions to afford the propargylic alcohol **3** which can be eventually deprotected to a versatile synthon, the terminal alkyne **4** [2,3]. Conjugated dinuclear complexes derived from racemic **2** or **4** can be used as models of molecular wires whose electronic behaviour is probed — after partial oxidation to the mixed-valent species — by spectroscopic analysis (UV–vis–NIR) [3]. Due to the chirality ($\Delta$ and $\Lambda$) of the metallic centres, the studies are performed on mixtures of stereoisomers (*meso*, $\Delta\Delta$, $\Lambda\Lambda$) that are experimentally indistinguishable by NMR, thus opening a debate on the influence of chirality on light-induced electron transfer. Undoubtedly, the isolation of compounds **2**–**4**

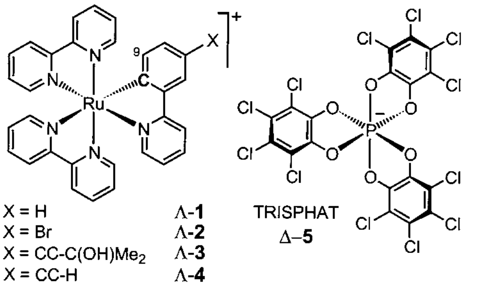

Fig. 1. Cyclometallated ruthenium complexes (**1**–**4**) and TRISPHAT anion (**5**).

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Table 1
Differences of chemical shift ($\Delta\delta_{max}$, $^1$H-NMR, 400 MHz, $CDCl_3$) observed for proton H(9) of the enantiomers of **2**–**4** by addition of $[Bu_4N][\Delta$-**5**]

| Entry | Complex | Equivalents | $\Delta\delta_{max}$ (ppm) |
|---|---|---|---|
| 1 | **2** | 0.95 | 0.039 |
| 2 | **2** | 2.1 | 0.046 |
| 3 | **3** | 1.1 | 0.045 |
| 4 | **3** | 2.5 | 0.049 |
| 5 | **4** | 3.2 | 0.042 |

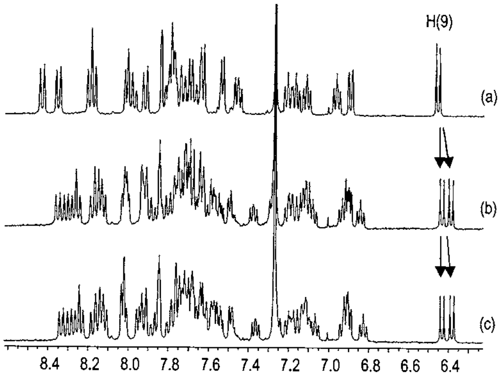

Fig. 2. $^1$H-NMR spectra (400 MHz, $CDCl_3$) of: (a) [*rac*-**3**][$PF_6$]; (b) [*rac*-**3**][$PF_6$] + 1.1 equivalents of [*n*-$Bu_4N$][$\Delta$-**5**]; (c) [*rac*-**3**][$PF_6$] + 2.5 equivalents of [*n*-$Bu_4N$][$\Delta$-**5**].

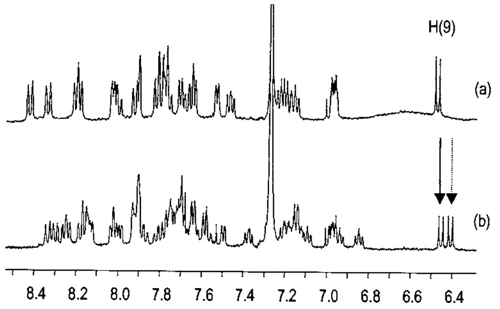

Fig. 3. $^1$H-NMR spectra (400 MHz, $CDCl_3$) of: (a) [*rac*-**4**][$PF_6$]; (b) [*rac*-**4**][$PF_6$] + 3.2 equivalents of [*n*-$Bu_4N$][$\Delta$-**5**].

in enantiopure form would be beneficial and this poses the problem of their resolution and the determination of their subsequent enantiomeric purity. So far, no such method has been described.

Chiral dicationic tris(diimine)ruthenium(II) complexes, which are extensively studied due to their interesting photochemical, photophysical and biological properties, can be — on the other hand — efficiently resolved by the formation of diastereomeric ion pairs with anionic chiral resolving agents; selective crystallisation [4] and/or ion-pair chromatography [5] resulting in the separation of the $\Delta$ and $\Lambda$ enantiomers. Recently, it has been shown that readily prepared and resolved tris(tetrachlorobenzenediolato)phosphate(V) anion **5** (or TRISPHAT [6]) is a useful diamagnetic NMR chiral shift agent [7] as well as a powerful resolving reagent (chromatography [8], asymmetric extraction [9]) for such dicationic complexes. The efficiency of the reagent **5** was explained by the formation of diastereomeric contact ion pairs between the chiral anions and cations; the short-range discriminating interactions leading to efficient magnetic non-equivalency and large differences in physical properties (elution, solubility) for the diastereomeric salts. It was therefore foreseen that anion **5** could behave as an NMR chiral shift reagent for the structurally related cations **2**–**4** and could lead possibly to their resolution. Herein, we show that it is indeed the case.

## 2. Results and discussion

### *2.1. NMR enantiomeric purity determination*

Racemic ruthenium(II) cyclometallated complexes **2**–**4** were thus studied in combination with a TRISPHAT salt (Table 1). In an NMR tube, [*n*-$Bu_4N$][$\Delta$-**5**] [10] was added as a solid to $CDCl_3$ solutions of the complexes until a satisfactory separation of some of the signals of the enantiomers ($\Delta\delta$) was observed (Figs. 2 and 3).[3] Efficient separation of the signals of **2**–**4** could be performed with a small amount of chiral shift reagent (0.95–3.2 equivalents, Table 1). Little difference could be observed between the spectra performed with the lowest and largest amounts (Fig. 2).

Proton H(9) of the cyclometallated ring is most easily monitored and a rather large difference in chemical shifts ($\Delta\delta_{max}$ ~ 0.045) is observed (Table 1). Sufficiently large magnetic non-equivalency was obtained, and the enantiomeric purity can be measured by the direct integration of the respective signals.

With this quantitative method of determination of the enantiomeric purity of complexes **2**–**4** in our hands, we turned our attention to the development of a resolution procedure.

### *2.2. Chromatographic resolution*

To resolve racemic complexes **2** and **4**, we used the ion-pair chromatographic conditions we reported earlier for the enantiomeric separation of configurationally stable dicationic ruthenium(II) tris(diimine) complexes [8]. The potential of anions **5** to serve as chromatographic resolving agents was first evaluated by analytical thin layer chromatography (TLC).

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[3] As no hydrogen atom is present on the anion, a rather large $^1$H-NMR spectral window ($\delta > 3.0$ ppm) is available for the analyses with [*n*-$Bu_4N$][$\Delta$-**1**].

Solutions of [cinchonidinium][*Δ*-**5**] (two equivalents, [6]) in acetone and of [*rac*-**2**][$PF_6$] or [*rac*-**4**][$PF_6$] in $CH_2Cl_2$ were prepared, mixed together, and the resulting solutions adsorbed on silica gel plates. Development by elution with $CH_2Cl_2$ showed a much-reduced affinity of salts [**2**][*Δ*-**5**] and [**4**][*Δ*-**5**] for silica gel, as they were retained to a much lower extent ($R_f$ ~ 0.7) than their $PF_6$ precursors ($R_f$ ~ 0) [11]. However, to our disappointment, only one band was observed. Based on our previous experience with tris(diimine) ruthenium(II) complexes, we had expected two bands corresponding to the separated diastereomers [9]. This negative result seemed to indicate a lack of chiral discriminations occurring between the TRISPHAT anion and the *Λ* and *Δ* enantiomers of the cations. Preparative column chromatography experiments ($SiO_2$, $CH_2Cl_2$, 10 × 1.5 cm) using mixtures of [cinchonidinium][*Δ*-**5**] (36 μmol), [*rac*-**2**][$PF_6$] or [*rac*-**4**][$PF_6$] (18 μmol) were performed and $^1$H-NMR analysis of the isolated [**2**][*Δ*-**5**] and [**4**][*Δ*-**5**] salts confirmed our analysis. The signals of both *Δ* and *Λ* enantiomers of the cations could be observed in a 1:1 ratio (Fig. 5, spectrum b).

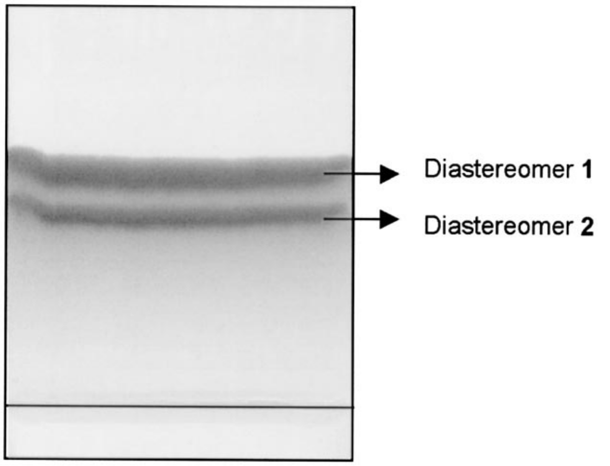

Fig. 4. Resolution by preparative TLC ($SiO_2$, 0.5 mm) of salt [**4**][*Δ*-**5**] using sequential elution of 20% $CH_2Cl_2$–benzene (2 × ) and then 30% $CH_2Cl_2$–benzene (2 × ).

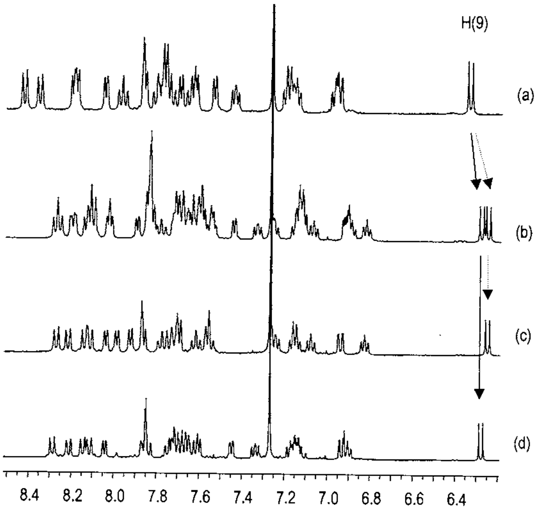

Fig. 5. $^1$H-NMR spectra (400 MHz, $CDCl_3$) of: (a) [*rac*-**2**][$PF_6$]; (b) [**2**][*Δ*-**5**] (1:1 ratio of diastereomers); (c) most eluted diastereomer; (d) least eluted diastereomer. Spectra b, c and d were performed with a minute amount of hydrazine in solution.

However, we noticed that these 1:1 mixtures of diastereomeric salts — [*Δ*-**2**][*Δ*-**5**]/[*Λ*-**2**][*Δ*-**5**] and [*Δ*-**4**][*Δ*-**5**]/[*Λ*-**4**][*Δ*-**5**] — exhibited a high solubility in low polarity solvents and in particular in mixtures of benzene and $CH_2Cl_2$. Considering that the migration of the salts with low polar benzene as an eluent could maximise the electrostatic attraction between the ions — and therefore increase the discriminating interactions — we decided to attempt the chromatographic resolution with mixtures of benzene and $CH_2Cl_2$ as eluents. The 1:1 mixtures of diastereomeric salts [**2**][*Δ*-**5**] and [**4**][*Δ*-**5**] were adsorbed onto preparative TLC plates ($SiO_2$, 0.5 mm, 20 × 20 cm). Sequential elution with 20% $CH_2Cl_2$–benzene (2 × ) and then 30% $CH_2Cl_2$–benzene (2 × ) afforded two well-separated bands (Fig. 4), which were abraded from the glass surface and stirred in $CH_2Cl_2$. The resulting suspensions were filtered and concentrated in vacuo.

$^1$H-NMR revealed two completely separated sets of signals corresponding each to the resolved *Λ* and *Δ* enantiomers of the cations (Fig. 5, spectra c and d). Pure separated diastereomeric ion pairs [*Δ*-**2**][*Δ*-**5**]/[*Λ*-**2**][*Δ*-**5**] and [*Δ*-**4**][*Δ*-**5**]/[*Λ*-**4**][*Δ*-**5**] were afforded in good chemical yields (45–48 and ~ 30% for the most and least eluted diastereomers, respectively).

Due to the lower symmetry of cations **2** and **4** — compared to the $D_3$-symmetry of $[Ru(diimine)_3]^{2+}$ analogues — we have made no attempts at determining by circular dichroism (CD) which of the fractions correspond the homochiral [*Δ*-**2**][*Δ*-**5**]/[*Δ*-**4**][*Δ*-**5**] and heterochiral [*Λ*-**2**][*Δ*-**5**]/[*Λ*-**4**][*Δ*-**5**] salts. CD measurements and absolute configuration assignments will be reported later.

## 3. Conclusions

We have shown that the determination of the enantiomeric purity of substituted cyclometallated ruthenium bis(diimine) complexes can be done readily using [*n*-$Bu_4N$][*Δ*-TRISPHAT] as an NMR chiral shift reagent. A rather simple resolution protocol by preparative TLC was developed which allows an efficient separation of the *Δ* and *Λ* enantiomers of substituted cyclometallated ruthenium derivatives **2** and **4**, opening a route to new stereo-controlled organometallic structures.

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