

Application of TRISPHAT anion as NMR chiral shift reagent

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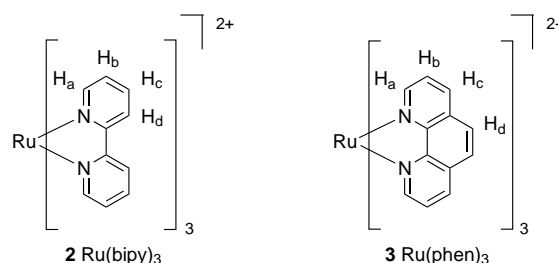
TRISPHAT anion **1** is an efficient NMR chiral shift reagent for cationic tris(bisimine)ruthenium(II) complexes.

Configurational stability¹ tris(bisimine)ruthenium(II) complexes have been extensively studied in the fields of photochemistry, photophysics and as probes in DNA. Many applications require these compounds in an enantioenriched form and thus determination of their optical purity is a necessity.² Herein, we report the application of TRISPHAT anion **1** as a useful chiral NMR shift reagent³ for two of these cationic complexes.

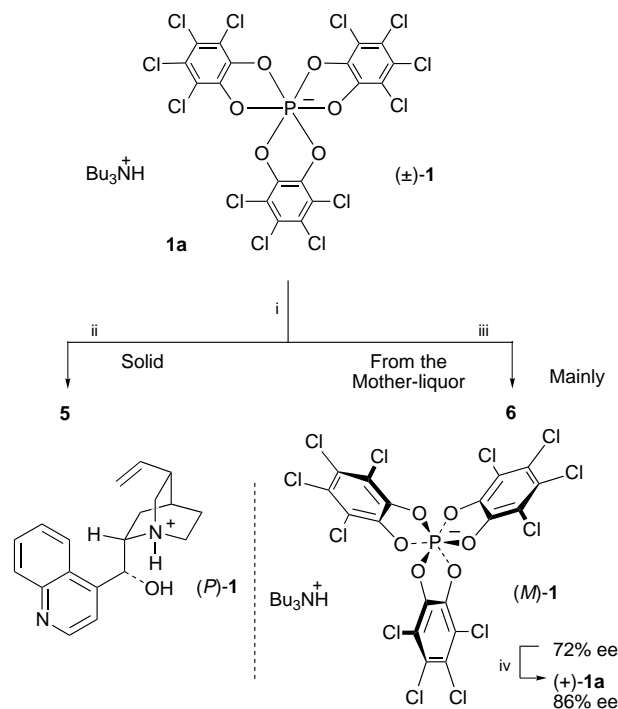
Recently, we have shown that chiral tris[tetrachlorobenzene-1,2-bis(olato)]phosphate anion **1** (or TRISPHAT) is configurationally stable in solution.⁴ It was foreseen that **1** would be an interesting NMR chiral shift reagent[†] for chiral cationic compounds, and tris(bisimine) complexes of transition metals in particular. Addition of enantioenriched **1** to solutions of tris(bisimine)ruthenium(II) compounds would lead to the formation of diastereomeric ion pairs, which have, at least in principle, different chemical shifts. Furthermore, as cations and anion **1** possess the same D_3 -symmetry, we thought that selective chiral discriminating interactions would likely occur, leading to a preferred association between the molecular propellers ($\Lambda^+ - \Lambda^-$ vs. $\Delta^+ - \Delta^-$). As a result, enantiotopic protons, carbon atoms and other nuclei of the cationic complexes would be resolved. We decided to test this hypothesis with Ru(bipy)₃ **2** and Ru(phen)₃ **3** complexes using Bu₃NH⁺-(*M*)-**1** salt [(+)-**1a**, 86% ee] as chiral shift reagent, which can be easily prepared as follows (Scheme 1). Addition of

0.5 equiv. of cinchonidine **4** to a solution of racemic tri-*n*-butylammonium salt [(±)-**1a**] in CH₂Cl₂ leads to the precipitation of a white solid **5** containing mainly cinchonidinium salts (72% de). Filtration and concentration of the mother liquor *in vacuo*, afford a white solid **6** containing the tri-*n*-butylammonium salt **1a** along with a minor amount of cinchonidinium salts. Recrystallisation of solid **6** in CH₂Cl₂-CHCl₃ affords, in the mother liquor, chemically and optically purified (+)-**1a** (86% ee).

Tris(bisimine)ruthenium(II) **2** and **3** were prepared as described by Broomhead and Young as dichloride salts (**2a**, **3a**).⁵ Racemic Ru(phen)₃Cl₂ **3a** was resolved by recrystallization with (+)-antimonyl tartrate anion;⁶ treatment of the tartrate or chloride salts with sodium perchlorate yielded the racemic or optically enriched [Ru(bipy)₃](ClO₄)₂·xH₂O (**2b**) and [Ru(phen)₃](ClO₄)₂·xH₂O (**3b**).[‡]



As foreseen, addition of 0.5–1.0 equiv. of (*M* or Λ)-TRISPHAT **1** to solutions of (±)-**2b** in CD₂Cl₂ ($1-2 \times 10^{-3}$ M), (±)-**3b** and (+)-**3b**⁷ in 7–10% DMSO in CD₂Cl₂ ($1-2 \times 10^{-3}$ M)[§] led to the resolution of the NMR spectra of the cations; we were able to distinguish between the two enantiomers and show that sample (+)-**3b** is optically pure. The resulting spectra at 400 MHz are shown in Figs. 1 and 2 and are compared to that of the same solutions in the absence of TRISPHAT. Upon addition of **1**, only the signals of one of the



Scheme 1 Reagents and conditions: i, 0.5 equiv. of **4**, CH₂Cl₂, 20 °C, 6 h; ii, filtration, **5** (44%); iii, concentration of the mother liquor *in vacuo* (60 °C, 10⁻⁴ bar, 12 h), **6** (55%); iv, (+)-**1a** (86% ee)

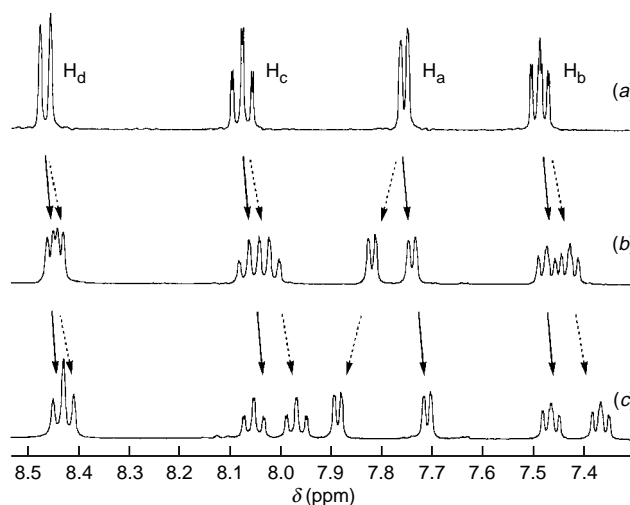


Fig. 1 The ¹H NMR spectra of racemic [Ru(bipy)₃](ClO₄)₂·xH₂O **2** in the absence (a) and presence of (+)-**1a** [0.5 equiv. (b), 1.0 equiv. (c)]

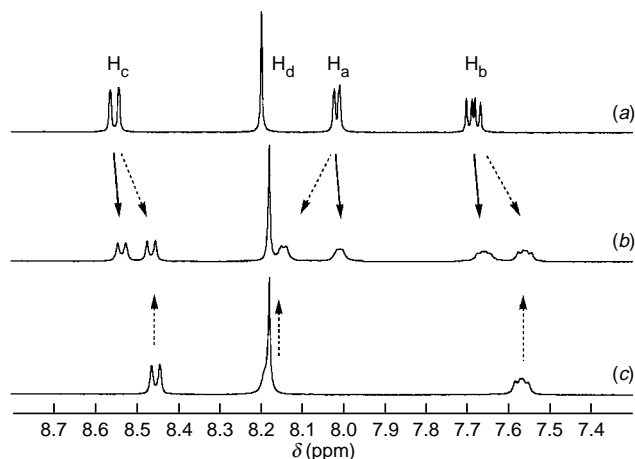


Fig. 2 The ^1H NMR spectra of $[\text{Ru}(\text{phen})_3(\text{ClO}_4)_2] \cdot x\text{H}_2\text{O}$ **3** in the absence (a) and presence of 1.0 equiv. of (+)-**1a**: (±)-**3b** (b) and (+)-**3b** (c). Spectra (a), (b) and (c) were done in 10, 10 and 7% DMSO in CD_2Cl_2 , respectively.

two enantiomers of **2** or **3** show strong shifts of its signals; observed chemical shifts (δ), upfield or downfield shifts induced by the phosphate reagent ($\Delta\delta$), and the magnitude of the difference in chemical shifts of analogous protons of the two enantiomers of **2b** and **3b** upon addition of the shift reagent ($\Delta\Delta\delta$) are summarized in Tables 1 and 2 respectively.

As is shown in Tables 1 and 2, substantial differences between analogous H_a , H_b , H_c protons of the enantiomers were found, while protons H_d in **2–3b** remain essentially unchanged. Proton H_a , the closest from the C_3 axis, has the largest difference between the signals, and it is shifted downfield contrary to that of the others. We feel that the larger $\Delta\Delta\delta$ of H_a and H_b and smaller $\Delta\delta$ of H_d are consistent with an ion-pairing model for anion induced shift, with cations and anions interacting most probably along their C_3 axes.

Finally, it is important to notice that the use of **1** as a NMR chiral shift reagent is not limited, in this case, by the presence of polar solvent such as DMSO or by non-coordinating ions.^{2a,b}

In summary, by addition of chiral anion **1**, we have observed differences in the chemical shifts of enantiomers of cationic species. We have used this technique to confirm enantiomeric

Table 1

Proton ^a	δ^b	δ^c	$\Delta\delta^c$	$\Delta\Delta\delta^c$		
H_a	7.758	7.889	7.712	0.131	−0.046	0.177
H_b	7.490	7.370	7.467	−0.120	−0.023	0.097
H_c	8.079	7.970	8.054	−0.109	−0.025	0.084
H_d	8.467	8.420	8.440	−0.047	−0.027	0.020

^a Chemical shifts for each enantiomer were assigned using a COESY experiment. ^b Without (+)-**1a**. ^c With 1.0 equiv. of (+)-**1a**.

Table 2

Proton ^a	δ^b	δ^c		$\Delta\delta^c$		$\Delta\Delta\delta^c$
		Λ^d	Δ	Λ^d	Δ	
H_a	8.015	8.144	8.009	+0.129	−0.006	0.135
H_b	7.684	7.559	7.658	−0.125	−0.026	0.099
H_c	8.554	8.464	8.536	−0.090	−0.018	0.072
H_d	8.198	8.180	8.180	−0.018	−0.018	0.00

^a Chemical shifts for each enantiomer of (±)-**3b** were assigned using a COESY experiment. ^b Without (+)-**1a**. ^c With 1.0 equiv. of (+)-**1a**. ^d Chemical shifts for Λ enantiomer in (±)- and (+)-**3b**.

purity of a complex. We think that this technique will be quite general for chiral cationic species. The observation that only one enantiomer of the cation shows a strong shift upon addition of **1** is also important. Further studies are being conducted to determine if this effect is due to a preferred association of the two molecular propellers, the nature of the interaction and its effectiveness for chiral recognition processes.

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Footnotes and References

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† More particularly in ^1H NMR spectra due to the lack of hydrogen atoms in **1**.

‡ The perchlorate salts were prepared to increase the solubility of the adducts in non-polar solvents.

§ Addition of DMSO (7–10%) is needed to insure the complete solubility of **3**. With 7% of DMSO in CD_2Cl_2 , protons H_a (Δ -isomer) and H_d are unfortunately isochronous.

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