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NMR enantiodifferentiation of thiiranium cations by chiral hexacoordinated phosphate anions[†]

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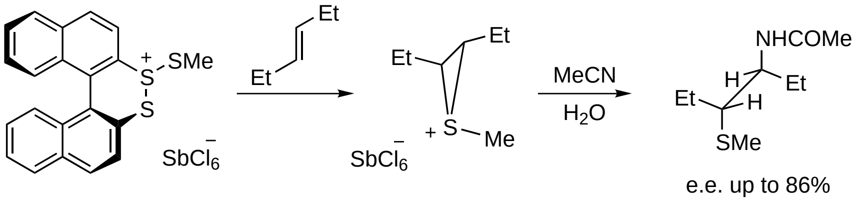
Abstract—BINPHAT anion—rather than TRISPHAT—is an efficient NMR chiral shift reagent for thiiranium ions such as *c*-2,*t*-3-di-*tert*-butyl-*r*-1-methylthiiranium and *t*-2-*tert*-butyl-*c*-3-phenyl-*r*-1-methylthiiranium cations. This is the first report on the NMR enantiodifferentiation of such chiral cations. © 2002 Elsevier Science Ltd. All rights reserved.

The stereoselective oxidative functionalization of unactivated C–C double bonds is a topic of great interest in today's chemistry. Whereas much activity has been devoted to the asymmetric transfer of oxygen and nitrogen atoms, attention has also been given to the addition of sulfur and selenium. Recently, diastereoselective additions of chiral selenium electrophiles, in which a stereogenic center is directly linked to the heteroatom, have been shown to be efficient processes.[1]

Previously, we reported the synthesis and the use of enantiopure chiral disulfides, which effectively mediate the asymmetric sulfenylation of prostereogenic alkenes (up to 86% e.e., Scheme 1); the chiral auxiliary being readily recovered from the reaction medium.[2] During the course of this study, the enantioselectivity of the reaction was determined on the final amino-sulfide products as no method could be found to analyze the enantiomeric purity[3] of the intermediate thiiranium ions generated by the transfer of 'RS^+' moieties from the enantiopure thiosulfonium ion to the carbon–carbon double bond (Scheme 1).[2]

We here report our preliminary results concerning the determination of the enantiomeric purity of thiiranium cations such as *c*-2,*t*-3-di-*tert*-butyl-*r*-1-methylthiiranium **1** and 2-*tert*-butyl-*c*-3-phenyl-*r*-1-methylthiiranium **2**[4] using BINPHAT **3** and TRISPHAT **4** anions as NMR chiral shift agents (Fig. 1).

Previously, the synthesis and resolution of tris(tetrachlorobenzenediolato)phosphate(v) anion or TRISPHAT **4** was reported.[5] This D_3-symmetric anion is an efficient NMR chiral shift, resolving and asymmetric inducing reagent onto organic and organometallic derivatives—with a predilection for octahedral metallo-organic complexes.[6] However, with some chiral C_2-symmetric cations, low NMR shifts and asymmetric inducing properties were observed. Assuming that its D_3-symmetry was not suitable for the chiral recognition



Scheme 1. Asymmetric azasulfenylation of C–C double bonds.

Keywords: NMR enantiodifferentiation; iranium ions; thiiranium ions; BINPHAT; TRISPHAT; chiral anions.

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[†] Dedicated to Professor Dr. Dr.h.C. Waldemar Adam on the occasion of his 65th birthday.

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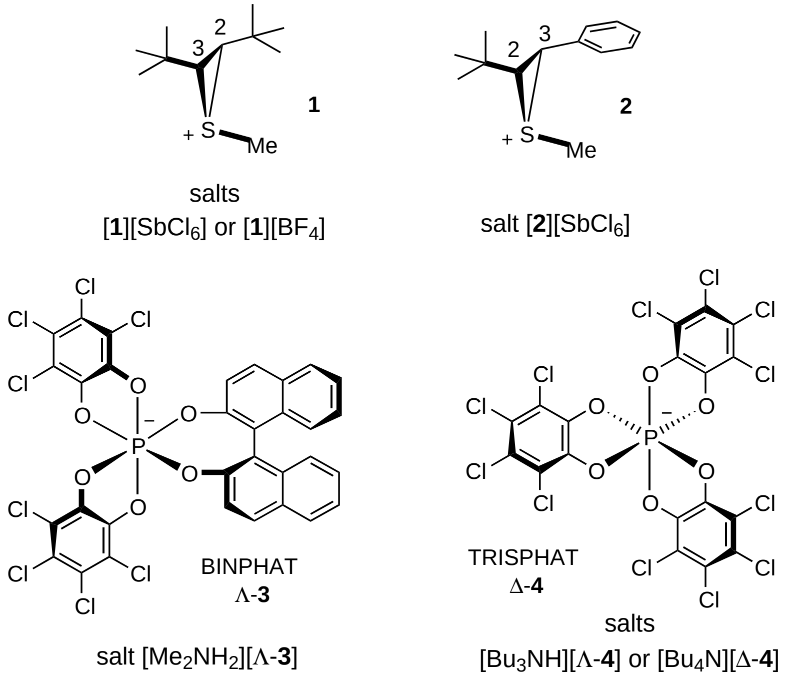

Figure 1. Chiral thiiranium ions **1** and **2** and anions BINPHAT **3** and TRISPHAT **4**.

of such cations, C_2-symmetric BINPHAT **3**—of configuration controlled by a BINOL ligand—was recently developed.[7] Higher level of asymmetric induction and better chiral shift properties were obtained using—in non-polar solvent conditions—this novel anion.

We chose for this study racemic *tert*-butyl substituted thiiranium ions **1** and **2**, salts [**1**][SbCl$_6$], [**1**][BF$_4$] and [**2**][SbCl$_6$], respectively, because of their greater stability with respect to less hindered thiiranium ions. We tested anions (Λ)-BINPHAT **3** and TRISPHAT **4**—of Δ or Λ configurations—as potential chiral shift reagents (Fig. 1); salts [Me$_2$NH$_2$][Λ-**3**], [Bu$_3$NH][Λ-**4**] and [Bu$_4$N][Δ-**4**] being used for this study.

^{1}H NMR spectra of di-*tert*-butyl substituted thiiranium salt [**1**][SbCl$_6$] in the absence of chiral shift reagents (a), in the presence of [Me$_2$NH$_2$][Λ-**3**] (b), of [Bu$_3$NH][Λ-**4**] (c) and of [Bu$_4$N][Δ-**4**] (d) are reported in Fig. 2. The addition of 0.5 equiv. of [Me$_2$NH$_2$][Λ-**3**] to a solution of [*rac*-**1**][SbCl$_6$] in CD$_2$Cl$_2$[8] (2.5–6.0$\times10^{-3}$ M) was performed at 250 K—to avoid eventual side-reactions between the acidic thiiranium cation and the phosphate anions or the known rearrangement of [**1**][SbCl$_6$][9]—and, as desired, the resolution of the ^{1}H NMR spectrum of cation **1** was achieved. All the signals were split in two separated sets. The signals pertaining to both enantiomers of cation **1** are shifted upfield even when using only 0.2–0.3 equiv. of [Me$_2$NH$_2$][Λ-**3**]. Observed chemical shifts (δ), upfield 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 [**1**][SbCl$_6$] upon addition of 0.5 equiv. of [Me$_2$NH$_2$][Λ-**3**] ($\Delta\Delta\delta$) are summarized in Table 1.

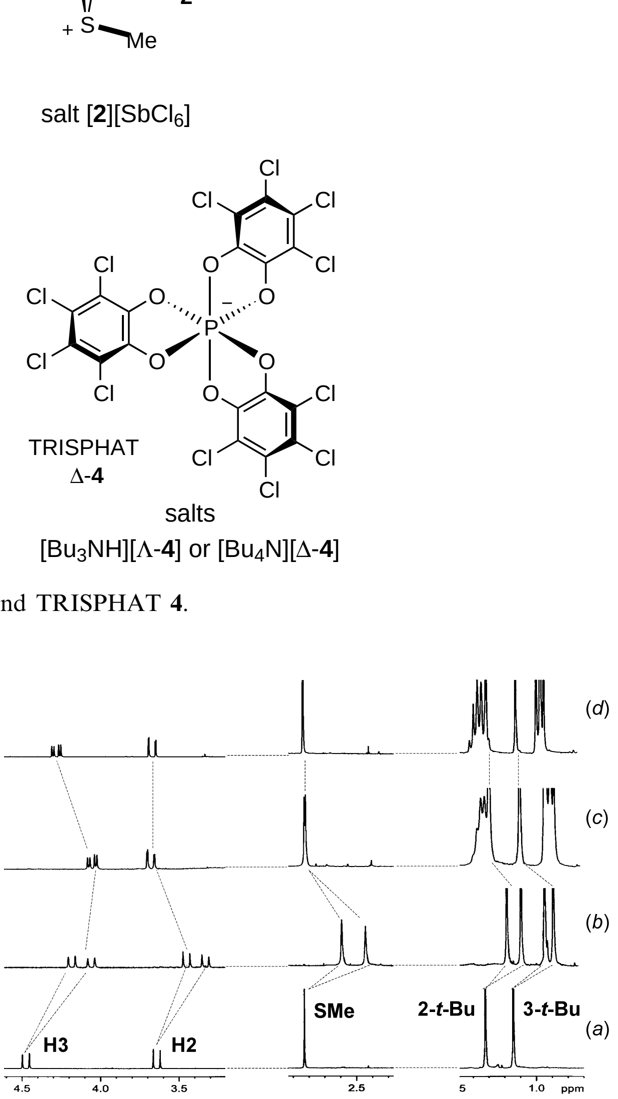

Figure 2. ^{1}H NMR spectra (300 MHz, 250 K, CD$_2$Cl$_2$, parts) for (a) thiiranium salt [**1**][SbCl$_6$], (b) [**1**][SbCl$_6$] and 0.5 equiv. of [Me$_2$NH$_2$][Λ-**3**], (c) [**1**][SbCl$_6$] and 1 equiv. of [Bu$_3$NH][Λ-**4**], (d) [**1**][SbCl$_6$] and 1 equiv. of [Bu$_4$N][Δ-**4**].

The efficiency of the splitting observed in the proton NMR, spectrum (b) in Fig. 2, suggests that the BINPHAT anion is most likely forming a contact ion pair with thiiranium cation **1**. The observed shifts of the signals in the presence of [Bu$_4$N][Δ-**4**] and [Bu$_3$NH][Λ-**4**] indicate that the discriminating interactions between cation **1** and TRISPHAT anion **4** are weaker. Thiiranium salt [**1**][BF$_4$] in the presence of [Me$_2$NH$_2$][Λ-**3**], [Bu$_4$N][Δ-**4**] or [Bu$_3$NH][Λ-**4**] salts behaves similarly to thiiranium salt [**1**][SbCl$_6$] indicating that the hexachloroantimonate or the tetrafluoroborate counterions do not influence the specific interactions between thiiranium cations and phosphate anions.

t-2-*tert*-Butyl-*c*-3-phenyl-*r*-1-methylthiiranium hexachloroantimonate salt [**2**][SbCl$_6$] was then studied

Table 1. Chemical shifts of thiiranium cation [**1**][$SbCl_6$] and effect on the chemical shifts induced by [Me_2NH_2][Λ-**3**] in CD_2Cl_2 at 250 K

Proton	δ^a	δ^b		$\Delta\delta^b$		$\Delta\Delta\delta^b$
H3	4.475	4.147	4.023	−0.328	−0.452	0.124
H2	3.642	3.416	3.296	−0.226	−0.346	0.120
SMe	2.828	2.557	2.407	−0.271	−0.421	**0.150**
2-*t*-Bu	1.322	1.150	1.060	−0.172	−0.262	0.090
3-*t*-Bu	1.144	0.911	0.855	−0.233	−0.289	0.056

[a] Without chiral anions.

[b] With 0.5 equiv. of [Me_2NH_2][Λ-**3**].

Table 2. Chemical shifts of thiiranium cation [**2**][$SbCl_6$] and effect on the chemical shifts induced by [Me_2NH_2][Λ-**3**] in CD_2Cl_2 at 250 K

Proton	δ^a	δ^b		$\Delta\delta^b$		$\Delta\Delta\delta^b$
H3	5.538	5.468	5.411	−0.070	−0.127	0.057
H2	4.334	4.336	4.320	+0.002	−0.014	0.012
SMe	2.110	2.055	1.800	−0.055	−0.310	**0.255**
t-Bu	1.244	1.189	1.132	−0.055	−0.112	0.057

[a] Without chiral anions.

[b] With 0.5 equiv. of [Me_2NH_2][Λ-**3**].

under similar experimental conditions. In Fig. 3 are reported the proton NMR spectra of salt [**2**][$SbCl_6$] in CD_2Cl_2 ($2.5–6.4\times10^{-3}$ M) at 250 K in the absence of chiral shift reagents (a), in the presence of [Me_2NH_2][Λ-**3**] (b), of [Bu_3NH][Λ-**4**] (c) and in the presence of [Bu_4N][Δ-**4**] (d). The NMR signals of the aromatic protons of [**2**][$SbCl_6$] are not reported since we could not observed any clear separations among them. ^1H NMR spectra of [**2**][$SbCl_6$] in the presence of [Me_2NH_2][Λ-**3**] show a complete splitting of the H3 doublet, of the SMe singlet and of the *tert*-butyl singlet, while the splitting of the H2 doublet is only partial. In Table 2 are reported the observed chemical shifts (upfield or downfield) induced by [Me_2NH_2][Λ-**3**] and the splitting (ΔΔδ) between analogous signals pertaining to the two thiiranium cation enantiomers. These combined data may suggest that the BINPHAT anion like to be closer to the *tert*-butyl side than to the phenyl side. TRISPHAT anions—salts [Bu_4N][Δ-**4**] and [Bu_3NH][Λ-**4**]—induce the complete splitting of the H3 doublet and only partial splitting of the other signals pertaining to the thiiranium ions enantiomers.

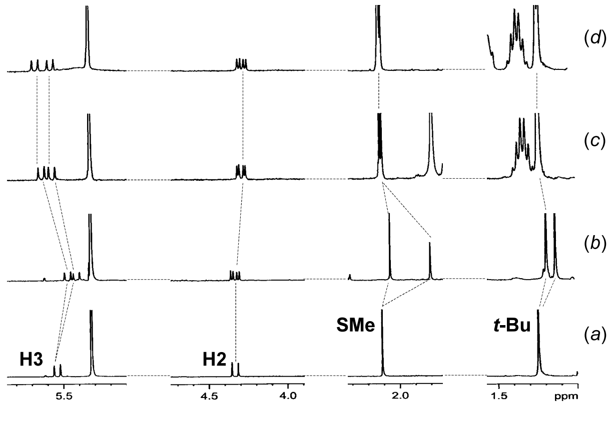

Figure 3. ^1H NMR spectra (300 MHz, 250 K, CD_2Cl_2, parts) for (a) thiiranium salt [**2**][$SbCl_6$], (b) [**2**][$SbCl_6$] and 0.5 equiv. of [Me_2NH_2][Λ-**3**], (c) [**2**][$SbCl_6$] and 1 equiv. of [Bu_3NH][Λ-**4**], (d) [**2**][$SbCl_6$] and 1 equiv. of [Bu_4N][Δ-**4**].

In conclusion, we have found that BINPHAT **3** is a very efficient chiral shift reagent for thiiranium cations having alkyl or aryl substituents. TRISPHAT **4** may also be used as a chiral shift agent but, in some cases, deconvolution of the signals might be necessary to correctly integrate the split signals. Further studies on the association between the thiiranium ions and BINPHAT anion are in progress to evaluate the potential of this method to the measure of face selectivity in asymmetric sulfenylation of C–C double bonds.

Acknowledgements

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