12-1-1997

Studies on Resolution of Enantiomeric Dialkylaryl Sulfonium Ions with NMR Shift Reagents

Ea-Ji-Ru Son
Western Kentucky University

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STUDIES ON RESOLUTION OF ENANTIOMERIC DIALKYLARYL SULFONIUM IONS WITH NMR SHIFT REAGENTS.

A Thesis

Presented to

the Faculty of the Department of Chemistry

Western Kentucky University

Bowling Green, Kentucky

In Partial Fulfillment

of the Requirements for the Degree

Master of Science

by

Son, Ea-Ji-Ru.

December 1997
STUDIES ON RESOLUTION OF ENANTIOMERIC DIALKYLARYL SULFONIUM IONS WITH NMR SHIFT REAGENTS.

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Acknowledgments

I would like to appreciate sincerely Dr. Thomas K. Green for directing this research and for his advice.

I would also like to thank Dr. John W. Reasoner and Dr. Lester L. Pesterfield for reviewing this thesis.

Finally, I would like to express my best appreciation to my parents in KOREA for their endless and devoted support.
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I. INTRODUCTION

Sulfonium ions are potentially chiral (asymmetric) in nature and they often occur as a pair of mirror-image stereoisomers, termed enantiomers. They are mirror images of each other but clearly different in that they are not superimposable. The same is true of some sulfonium ions, as shown below (Figure 1).

![Figure 1. Two nonsuperimposable mirror-images of ethylmethylphenylsulfonium ion](image)

These sulfonium ions possess a chiral center at the sulfonium group and may be expected to act as a chiral alkylating agents for carbon nucleophiles in asymmetric alkylation of $\beta$-keto esters.\(^1\)

Ordinarily, enantiomers cannot be distinguished by NMR spectroscopy. One method of resolving them is to couple them to a chiral NMR shift reagent. The shift reagent interacts with the sulfonium ion to cause a dispersion of the peaks in the spectrum. An ordinary shift reagent is not enough, however; the shift reagent must also be chiral and enantiomerically
The idea is that one enantiomer of the mixture of sulfonium ions interacts more strongly with the chiral shift reagent than the other enantiomer. Assuming that sulfonium ions are present as a racemic mixture of $S(\, +)$ and $S(\, -)$, the addition of a pure enantiomer of a chiral shift reagent results in the formation of two diastereomeric complexes. If, for example, the lanthanide shift reagent is $L(\, -)$, we obtain:

$$S(\, +) + L(\, -) \rightarrow S(\, +)L(\, -)$$

$$S(\, -) + L(\, -) \rightarrow S(\, -)L(\, -)$$

In the complexes thus formed, the enantiomers $S(\, +)$ and $S(\, -)$ can be distinguished by their different resonance, which results in a resolution of two enantiomers of the sulfonium ion in the NMR spectrum.

A. Enantiomeric purity Regulation and Measurements.

Because of the inherent chirality (or handeness) of nature, most biological systems recognize different enantiomers as different substances. As a result, the majority of chiral drugs must now be administered in an enantiomerically pure form since each enantiomer may have widely varying properties in the body.

Over the past decade there has been great interest in enantioselective synthesis which has led to an increased demand for accurate, reliable, and convenient methods of measuring enantiomeric purity. Before the mid-1960s, the enantiomeric purity of a chiral molecule was usually assessed by using chiroptical methods which often involved measuring the optical rotation of the sample with the use of a polarimeter under defined conditions of temperature, solvent, and concentration and at a given wavelength of the incident plane-polarized light. This value was then compared to the known rotation for an enantiomerically pure sample of the same compound, measured under identical conditions. This value is commonly termed
"optical purity." Provided that the measurement is carried out under rigorously controlled conditions along with appropriate calibrations, then this value may be equated with "enantiomeric purity." There are two major problems with this method of analysis. First, optical purity and enantiomeric purity are not necessarily equivalent. It has been demonstrated that optical rotation does not vary linearly with enantiomeric composition for 2-methyl-2-ethyl-butanoic acid in various nonpolar solvents. Although in this case diastereoselective dimerization is the likely cause of the "nonideal" behavior, there are reports of nonlinear variations of optical rotation with concentration even in polar solvents. A second limitation is that the literature is populated with many examples of incorrect rotations for compounds considered to be enantiomerically pure. For example, prior to 1974, the specific rotation of enantiomerically pure (+)-3-methylcyclopentene was believed to be $[\alpha]^{20}_D = +78^\circ$ Following an independent measurement using a chiral gas chromatographic method, the rotation was shown to be $[\alpha]^{20}_D = +174.5^\circ$ for the enantiopure compound. More recently, the enone, as shown below, has been shown to have a rotation of $[\alpha]^{20}_D = +34^\circ \text{(CHCl}_3)$, whereas its enantiomer has been reported to have a rotation of $[\alpha]^{20}_D = -115.4^\circ \text{(CHCl}_3)$.

Also, there have been reports of incorrect interpretation of literature rotations. The rotation of enantiopure exo-2-norbornane-carboxylic acid is $[\alpha]^{20}_D = -27.8 \text{ (EtOH)}$. Unfortunately, it was assumed that this value should be $[\alpha]^{20}_D = -10.7 \text{ (EtOH)}$ so that
incorrect enantiomeric purities have been reported for the asymmetric hydrocyanation of norbornene (subsequently corrected following an independent NMR analysis using a chiral derivatizing agent) and for the asymmetric hydroformylation of norborane.\textsuperscript{8-10} Finally, the use of optical rotation for determination of enantiomeric purity is subject to the uncertainty of contamination with an optically active impurity. The uncertainty is particularly serious if the impurities have a high rotation or a rotation of the opposite sign to that of the substrate being analyzed. Certainly sample homogeneity must be demonstrated in parallel with the measurements of rotation, and the quoted values should include error limits. Although the method is a convenient one it is rather unsatisfactory for determining accurate enantiomeric purity unless stringent control conditions are followed.

Given these limitations, it is necessary to use independent methods of analysis when measuring enantiomeric purity. Although rapid progress has been made in developing sensitive and accurate GC and HPLC methods of analysis, many practicing organic chemists use NMR methods.\textsuperscript{11,12} Gas chromatographic methods are preferred for quality control in pharmaceutical and fine chemical applications, being more precise than the NMR-base methods. The HPLC methods of chiral analysis are also used to an increasing extent as a result of improvements in column lifetime and performance.

B. Lanthanide NMR Shift reagents (LSRs).

1. Fundamentals: Lanthanide NMR shift reagents have become extremely valuable tools in a relatively short period time. The potential user of NMR shift reagents needs to know what types of information can be obtained from their use and how this information can be used in solving problems of chemical importance. The most commonly used shift reagents are lanthanide \( \beta \)-diketonates. The LSRs are composed of \( \beta \)-diketonate ligands coordinated
to lanthanide cations such as Eu$^{3+}$, Pr$^{3+}$, Yb$^{3+}$.	extsuperscript{13} These cations which are paramagnetic have short electron-spin relaxation times, and the problems associated with line broadening are minimal. The fluorinated chelates ligands are also much more effective chemical shift reagents than unfluorinated chelates because they are stronger Lewis acids. Two common examples of LSRs are Eu(dpm)$_3$ and Eu(fod)$_3$, where dpm is the tris-dipivaloylmethanato derivative and fod is the tris 6,6,7,7,8,8-heptafluoro-2,2-dimethyloctanetonato derivative. The structure of these compounds are shown below.\textsuperscript{14}

Table 1 represents a list of $\beta$-diketonates that are commonly used as ligands. Three fundamental properties of the lanthanide cations are their Lewis acid characteristics, their unpaired $f$ electrons and their tendency to coordinate with different substrates with coordination number between 8 and 10. They function by acting as Lewis acids, forming a complex with the substance under analysis, which acts as a Lewis base. A reasonably large number of different combinations of $\beta$-diketones and lanthanides can serve as shift reagents. In the earliest studies, complexes of the thd ligands [tris(2,2,6,6-tetramethyl-3,5-heptanedione)] were usually employed.

Morrill \textit{et al.} have proposed the hard-soft acid-base (HSHB) theory as an indicator.
Table I. Various $\beta$-diketonates ligands used in lanthanide shift reagents.

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<tr>
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<th>Structure</th>
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<td>H(acac)</td>
</tr>
<tr>
<td>1,1,1-Trifluoro-2,4-pentanedione</td>
<td><img src="#" alt="Structure" /></td>
<td>H(tfa)</td>
</tr>
<tr>
<td>1,1,1,5,5,5-hexafluoro-2,4-pentanedione</td>
<td><img src="#" alt="Structure" /></td>
<td>H(hfa)</td>
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<td><img src="#" alt="Structure" /></td>
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<td>Compound</td>
<td>Structure</td>
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</tr>
<tr>
<td>1,1,1,5,5,6,6,7,7,7-Decafluoro-2,4-heptanedione</td>
<td><img src="image1" alt="Structure1" /></td>
<td>H(dfhd)</td>
</tr>
<tr>
<td>4,4,4-Trifluoro-1-(2-thienyl)-1,3-butanedione</td>
<td><img src="image2" alt="Structure2" /></td>
<td>H(tta)</td>
</tr>
<tr>
<td>4,4,5,5,6,6,6-Heptafluoro-1-(2-thienyl)-1,3-hexanediol</td>
<td><img src="image3" alt="Structure3" /></td>
<td>H(hfth)</td>
</tr>
<tr>
<td>3-(Trifluoroacetyl)-(\delta)-camphor</td>
<td><img src="image4" alt="Structure4" /></td>
<td>H(tf(\delta))</td>
</tr>
<tr>
<td>3-(heptafluoro-butryl)-(\delta)-camphor</td>
<td><img src="image5" alt="Structure5" /></td>
<td>H(hf(\delta))</td>
</tr>
</tbody>
</table>
of expected interaction of shift reagent with substrates. They found that the degree of interaction of organo-sulfur compounds was proportional to the polarizability (HSAB character) of the nucleophile functionality. The LSR compounds with lanthanide cations $3^+$ charge are assumed to be hard acids which tend to coordinate more strongly with hard substrates. Therefore, LSR compounds are not useful in the analysis of soft substrates such as thioesters, mercaptans, nitrocompounds, alkenes, and aromatic hydrocarbons. The weak interaction of these reagents with LSR compounds results from the substrate containing highly polarizable Lewis base sites.

A study of seven amines showed that those with the most steric hinderance exhibited smaller magnitudes of induced shifts in comparison with less hindered amines. The effects of steric hinderance are also apparent in the case of $N, N$-dimethylaniline, which show greatly reduced induced shifts even though they are more basic than aniline.

There are three general requirements for LSRs. First, they should be soluble in nonpolar organic solvents. Second, they should be capable of interaction with a large number of substrates (based on acidic or basic properties); and, third, they provide optimal shifting potential combined with minimal line broadening effects. Substitution by the more electron-withdrawing fluorines in the fluorinated chelates ligands enhances the acidity of the chemical shift reagents which makes them more able to coordinate with relatively weak Lewis bases. Another advantage of these LSRs is the comparatively small extent of interfering signals in the NMR spectra. It is of course necessary to dry the shift reagent before using (as hydrolysis leads to formation of Eu$_2$O$_3$ and severe line broadening), although sublimation ($200^\circ$C, 0.05 mmHg) is preferred. Therefore, any impurities like water could prevent the substrate from occupying coordination sites on the lanthanide cation. CDCl$_3$, CCl$_4$, and C$_6$H$_6$ are the suitable
solvents for lanthanide induced shift studies. The solvents $d_6$-acetone, and $d_6$-dimethyl sulfoxides are not useful for use with lanthanide shift reagents, because they are capable of bonding effectively to lanthanide ions. One of the important advantages of Eu-LSRs over the other types of chemical shift reagents is that minimum crossovers in induced shifts occur. As a result, overlapping between induced signals is minimized.

Addition of a lanthanide shift reagent to an organic compound can cause the shifts of resonances to higher (or lower) frequency, the size of which is determined primarily by the distance of the given type of proton from the donor group. The six-coordinate lanthanide complex forms a weak addition complex with a large variety of organic compounds that is in fast exchange with the unbound organic substrate on the NMR time scale. The induced shifts are caused by a large difference in the magnetic susceptibility tensors for the seven-coordinate complex and the McConnell-Robertson equation $\Delta \delta = K(1-3\cos^2\theta)r^3$, which will be discussed later, qualitatively defines the relationship between the induced chemical shift of the nucleus and the location of the nucleus. The position of a given peak is consequently related to the stability of the complex formed, the amount of shift reagent added, and the McConnell-Robertson equation.

Lanthanide-shift reagents are in general less useful at high fields. Under the fast exchange conditions that typically prevail, line broadening is proportional to $B_0^2$, and for substrates that show large induced shifts (e.g., alcohols) it is preferable to acquire spectra on a 100-MHZ $^1$H instrument, rather than a 500-MHZ instrument where line broadening will be 25 times more severe.

Most applications involve $^1$H NMR analysis, but $^{13}$C, $^{19}$F, and $^{31}$P are commonly used. It remains a mystery why Eu(tfc)$_3$ and Eu(hfc)$_3$ are used almost exclusively, when Pr(hfc)$_3$ and
Yb(hfc), offer distinct advantages.\textsuperscript{22-25} Provided that care is taken in data acquisition and manipulation (aided for example by the use of Gaussian line narrowing methods and base line correction routines), accurate values of enantiomeric purity may be obtained.\textsuperscript{26} In the range 40 to 60 \% e.e., the best claimed deviation is \(\pm 2\) \%,\textsuperscript{27} although a note of caution is required for e.e. values \(\geq 90\) \%, where the error is reported to be on the order of 10 \%.\textsuperscript{28}

2. Chiral Shift Reagents and Applications: Although enantiomers cannot be distinguished in an achiral medium, since the resonances of enantiotopic nuclei are isochronous, diastereoisomers may be distinguished because the resonances (of certain diastereotopic nuclei) are anisochronous. The chemical shift nonequivalence of diastereotopic nuclei in diastereoisomers in which the stereogenic centers are covalently linked in a single molecule was first noted by Cram.\textsuperscript{29} The determination of the enantiomeric purity using NMR therefore requires the use of a chiral auxiliary that converts the mixture of enantiomers into a diastereoisomeric mixture. As long as there is a large enough chemical shift nonequivalence to give baseline resolution of the appropriate signals, then integration gives a direct measure of diastereomeric composition which can be related directly to the enantiomeric composition of the original mixture. Resonances of enantiomers undergo different chemical shifts in a chiral environment, leading to determination of enantiomeric relative abundances.

To determine enantiomeric compositions by use of chiral shift reagents, one must chose one or more signals to monitor for enantiomeric shift differences, or different shifts, \(\Delta \delta\).\textsuperscript{30} A general guideline for choosing such signals is that they show sufficient response to the shift reagent and be adequately separated from other signals.\textsuperscript{31} A good discussion of practical use of these reagents, such as the selection of solvents and sample preparation, has been presented by McCreary \textit{et al.}\textsuperscript{32}
The ability of chiral shift reagents to cause differential shifts in protons or groups which are enantiotopic by internal comparison, i.e., enantiotopic protons or groups on the same molecule, has been reported by Fraser et al. They found that Pr(hfc)$_3$ induced a chemical shift difference for the CH$_2$ protons of benzyl alcohol, allowing determination of the germinal coupling constant. No significant change in the value of the coupling constant occurred until 0.3 equivalent of shift reagent had been added. Addition of Pr(hfc)$_3$ also distinguished methyl groups of dimethyl sulfoxide and 2-propanol which are enantiotopic by internal comparison. Goering et al. reported that Eu(hfc)$_3$ induced differential shifts in enantiotopic protons of six substrates, while Eu(tfc)$_3$ induced such an effect in one case.

Polar substrates like chiral 1,2- and 1,3-diols are easily managed to analysis in $d_3$-acetonitrile as NMR solvent. For example, the nonequivalence of the enantiotopic C-2 hydroxy resonances in 3-chloropropane-1,2-diol have been observed by using CLSRs (Chiral Lanthanide Shift Reagents). Chiral carboxylic acids are usually not tractable to direct analysis in this manner. They may either be converted into their corresponding tertiary amides (amides are good $\sigma$-donors for europium or ytterbium) or may be examined directly in aqueous solution. The methyl resonances of several $\alpha$-hydroxycarboxylates have been resolved in the presence of EuCl$_3$ (or PrCl$_3$) and 3 equivalent of enantiopure citramalate or malate. A useful $^1$H NMR method for the analysis of chiral alkanes, arenes, and allenes has been made. It uses a mixture of Yb(hfc)$_3$ and the achiral silver shift reagent Ag(fod) following an initial report that used Eu(tfc)$_3$ and silver trifluoroacetate for chiral alkene analysis. A mixed complex forms in solution and the chiral hydrocarbons interact weakly with silver ion and induced shifts are observed. Chemical shift nonequivalence for diastereotopic nuclei was
typically $\Delta \delta_H$ (CDCl$_3$, 298 K)=0.3 to 1.00 ppm for chiral alkenes, 0.3 ppm for chiral allenes (Figure 2).

Consequently, one can use chiral shift reagents to determine whether reactions have occurred with retention of configuration, inversion, racemization or some combination. Protons and groups which are enantiotopic by internal comparison also show separation of resonances in the presence of a chiral shift reagent, and this fact can be useful to differentiate meso from dl diastereomers.

Figure 2. $^1$H NMR chemical shift nonequivalence ($\Delta \delta_H$, ppm, CDCl$_3$) observed with use of Yb(hfc)$_3$/Ag(fod) and substrates shown.

C. Historical Background for applications of LSRs

In 1969, Hinckey found that the dipyridine adduct of Eu(thd)$_3$ [Eu(thd)$_3$ = tris(2,2,6,6-tetramethyl-3,5-heptanedionato)europain(III), also called Eu(dpm)$_3$, where Eu(dpm) tris(dipivaloylmethanato)europain(III)] induced shifts in the NMR spectrum of cholesterol monohydrate. Sanders and Williams then found that unsolved Eu(thd)$_3$ was even more
effective as a shift reagent than the dipyridine adduct, inducing shifts up to four times as great in magnitude.\textsuperscript{49}

In 1971, Rondeau and Sievers reported that shift reagents that contained the fluorinated ligand, 6,6,7,7,8,8,8-heptafluoro-2,2-dimethyl-3,5-octadione, Eu(fod)\textsubscript{3} and Pr(fod)\textsubscript{3}, were superior to Eu(thd)\textsubscript{3} in clarifying spectra.\textsuperscript{50} It was Whitesides and Lewis who first demonstrated the application of chiral lanthanide shift reagents in enantiomeric purity determination.\textsuperscript{51} By using the chiral europium complex Eu(pvc)\textsubscript{3} (pvc=3-pivaloyl-\textit{d}-camphor) well resolved signals for the methyl, methine, and ortho aromatic protons of \textalpha-phenylethylamine, as shown in Figure 3, were observed for each of which a large induced shift was observed.

Following the early work of Whitesides with the camphor-based chemical shift reagent Eu(pvc)\textsubscript{2}, several other chiral shift reagents were introduced (Table II), many of which are available commercially.\textsuperscript{51}

The dicamphoyl reagent Eu(dcm)\textsubscript{3} exhibits the best differential shift dispersion, and Eu(hfc)\textsubscript{3} gave particularly large \(\Delta \delta\) values for its diastereoisomeric complexes with chiral substrates in \textsuperscript{13}C rather than in \textsuperscript{1}H NMR. The praseodymium complex Pr(hfc)\textsubscript{3} performs better than Eu(hfc)\textsubscript{3} in \textsuperscript{1}H NMR giving the largest \(\Delta \delta\) values at lowest concentration of added shift reagents, while Yb(hfc)\textsubscript{3} has been shown to be superior to Pr(hfc)\textsubscript{3} in the analysis of a series of chiral sulfoxides.\textsuperscript{52} The praseodymium shift reagents offer the possible advantage (e.g., in analysis of diastereotopic methyl groups) that induced shifts are to lower frequency, rather than to higher frequency as noted for the europium and ytterbium complexes. This phenomenon has been used to good effects in the determination of the enantiomeric purity of carboxylates. By using the achiral shift reagent tris(tetraphenylimidodiphosphinato)prase-
Figure 3. 100-MHz proton NMR spectra of a CCl₄ solution Eu(pvc)₃ and (S)-α-phenylethylamine (upper) and of a mixture of (R)- and (S)-α-phenylethylamine (lower).
odymium(III), Pr(tpip)$_3$\cite{55,56} the adducts formed with potassium salts of chiral carboxylic acids are in slow exchange on the NMR time scale and form dinuclear complexes.\cite{57}

**Table II. Common chiral lanthanide shift reagent**

<table>
<thead>
<tr>
<th>structure of L in LnL$_3$</th>
<th>lanthanon abbreviation*</th>
</tr>
</thead>
<tbody>
<tr>
<td>[Diagram of Eu Eu(tpip)$_3$]</td>
<td>Eu Eu(tpip)$_3$</td>
</tr>
<tr>
<td>[Diagram of R = CF$_3$]</td>
<td>Eu Eu(tfcl)$_3$ Pr Pr(tfcl)$_3$ Yb Yb(tfcl)$_3$</td>
</tr>
<tr>
<td>[Diagram of R = C$_3$F$_7$]</td>
<td>Eu Eu(hfc)$_3$ Pr Pr(hfc)$_3$ Yb Yb(hfc)$_3$ Eu Eu(dcm)$_3$</td>
</tr>
</tbody>
</table>

*pvc = pivaloyl-d-camphorato; tfc = trifluorohydroxy-methylene-d-camphorato; hfc = heptafluorohydroxy-methylene-d-camphorato; dcm = dicamphoyl-d-methanato.

Thus a racemic 2-phenylbutyric acid gives rise to diastereomeric complexes (SS/RR and RS) which are clearly distinguished in $^1$H NMR (CD$_2$Cl$_2$) (Figure 4) and are shifted to lower frequency.

![Figure 4. $^1$H NMR spectrum of the two diastereomeric complexes obtained from Pr(tpip)$_3$ and 2-phenylbutyrate (CD$_2$Cl$_2$, 293 K)](image)
The use of shift reagents for distinguishing isomers is widespread. Glove and Pointer were able to estimate proportions of two isomeric methylated imidazoles by making use of the fact that for one isomer, steric hinderance prevented strong complexation with the shift reagent. Addition of Eu(thd)$_3$ or Eu(fod)$_3$ led to separation of resonances, as one isomer experienced shifts and the other did not. Corfield and Trippett measured lanthanide-induced shifts in cis and trans isomers of 2,2,3,4,4-pentamethylphosphetan oxides (Figure 5). The set of isomers that was known or assumed to be cis showed one range of shifts for the 3-protons, while the set known or assumed to be trans gave another range of shifts for the same proton resonance. Shifts for other protons were less definitive, but a consistent difference between the two sets was observed. Thus the shifts of an unknown isomer could be compared with these results and its configuration assigned.

Figure 5. Cis and Trans isomers of 2,2,3,4,4-pentamethylphosphetan oxides.

Sandere and Williams reported that functional groups gave magnitudes of induced shifts which decreased as -NH$_2$ > -OH > C=O > O->-CO$_2$R > -CN. Thiols, thioethers, and acyl
phosphines generally have less interaction with the lanthanide than oxygen and nitrogen analogs.\textsuperscript{60} A series of inter- and intra-molecular competition experiments in the presence of shift reagent has been done by Hart and Love.\textsuperscript{61}

Ahmad \textit{et al.} have investigated the temperature dependence of shift reagents. Proportional enhancement of all signals in the substrate was observed as the temperature dropped to -30°C. The observation suggests the possible utility of reduced temperature determinations where the solubility of lanthanide complex is not adequate.\textsuperscript{62}

Many papers have been published on the application of LSRs in order to derive stereochemical information from chemical shift data. Current textbooks and lab manuals also include the use of LSR as a part of the standard NMR techniques.

From the above examples it is clear that much stereochemical data can be obtained with a minimum of time and effort by adding shift reagents.

\section*{D. General nature and Magnetic interaction between LSRs and Organic molecules}

The mechanism of binuclear complexes resulting from LSRs and substrate is not completely understood.\textsuperscript{63} However, since the effects are related to the presence of paramagnetic ions, it is reasonable to suppose that it involves an interaction between the nuclear spins and the spin of the unpaired electron. It is believed that there are two types of interactions that are responsible for the observed shifts: namely contact interaction and the pseudo contact interaction. Both depend on the formation of a complex between the substrate S and the paramagnetic metal ion L; in solution an equilibrium is established between the free components and the complex:
In the complex some of the spin density of the unpaired electron becomes transferred to the substrate molecule owing to the contact interaction. As the electron spin densities at the positions of the nuclei under observation are widely different, the resulting shift effect is not the same through the molecule.

In saturated compounds the $^{13}$C nuclei whose resonance positions are most affected are those at the $\alpha$- and $\beta$-positions relative to the complexing center (e.g. O, N, or S), whereas in conjugated systems, as a result of the greater degree of delocalization of the spin density, the resonances of more distant $^{13}$C nuclei are also affected. Also one expects to find significant differences between the shifts for $^1$H and $^{13}$C resonances. The contact interaction involves a coupling of molecular orbitals and is observed for transition metal shift reagents where unpaired electrons are in d orbitals. These reagents are involved in covalent bonding with a substrate. Contact shifts are unpredictable and can be calculated only by detailed MO (Molecular Orbital) treatments. For lanthanides the unpaired electrons are in the 4f orbitals, which are shielded by the filled 5s and 5p orbitals. These unpaired electrons cannot form covalent bonds with substrate molecules. In the lanthanide, only electrostatic interactions are observed between the metal and ligands. As such, the probability of finding the unpaired metal electron near the nuclei of the substrate is relatively low. This probability decreases rapidly from the site of complexation; therefore, a pseudo contact shift mechanism is dominant. The contact term is usually negligible in $^1$H NMR spectroscopy, but this is not the case for $^{13}$C NMR spectroscopy.

More detailed structural and stereochemical information may be obtained by the application of the McConnell-Robertson equation (Equation 1), which shows the relationship between the induced chemical shift of the nucleus and the location of the nucleus. Here $K$ is
\[ \Delta \delta_{LSR.S} = \frac{K(3 \cos^2 \theta - 1)}{r^3} \]

Equation 1.

A constant, \( r \) is the distance from the nucleus to the lanthanide ion, and \( \theta \) is the angle between the principal magnetic axis of the complex, usually assumed to be essentially colinear with the lanthanide-nucleophile bond axis, and a line drawn from the nucleus of interact to the lanthanide ion:

\[ \text{O—C} \]

The use of McConnell-Robertson equation includes several assumptions, usually taken to be

i) The observed shifts used in the analysis are entirely pseudo-contact in origin.

ii) Only one stoichiometric species exists in solution in equilibrium with the uncomplexed substrate.

iii) Only one geometric isomer of this species is present.

iv) This isomer is magnetically axially symmetric, so that the shifts are proportional to the geometric factor: \( K(3 \cos^2 \theta - 1)r^{-3} \).
v) The principal magnetic axis has a particular, known orientation with respect to the substrate ligand or ligands.

vi) The substrate ligand exists in a single conformation, or an appropriate averaging over internal motions is performed.

Horrocks has suggested that even if axial symmetry of the complex does not exist in the crystal, the averaged effect of rapidly interconverting geometrical isomers in solution leads to shifts approximating those which would be obtained from axial model.\(^5^8\)

The angle term in equation 1 gives positive values, except when \(\theta\) is greater than 55°, but less than 125°. At these angles induced shifts will be in the opposite direction to the normal shifts, e.g., upfield for Eu and downfield for Pr. As shown in Figure 6, this reversal in the direction of the shift corresponds to the term \(3\cos^2\theta-1\) becoming negative for this range of angles which accounts for the occasional observation that as one adds a shift reagent such as \(\text{Eu(fod)}_3\), most peaks are shifted downfield, but some shift upfield or remain unchanged. Initial reports frequently neglected the angle term, considering distance only, but the importance of including the term has been documented by many workers. An example of the effects of the angle dependence on shifts has been given by Rondeau and Berwick, who used \(\text{Eu(fod)}_3\) to determine isomeric composition of the mixture of \(p, p\)-disubstituted azoxybenzenes.\(^6^0\) The two geometrical isomers are shown in Figure 7. A scale model was used to estimate the H-Eu-O angles for the methoxy amd methyl protons of one isomer (Figure 8). If one assumes that the Eu-O bond length is approximately 2 Å, the angle made with the methoxy protons is 84° and the angle with the methyl protons is 40°, for this isomer.
Figure 6. The variation of $3\cos^2\theta - 1$ with the angle $\theta$. 
Consequently, as predicted from the McConnell-Robertson equation, the methyl peak is shifted downfield ($\theta > 55^\circ$). In the second isomer, the position of the oxygen, and consequently the europium, causes the reverse for the methoxy and methyl protons because of changes in $\theta$. The spectra shown in Figure 7 illustrate this phenomenon for the mixture of the two geometrical isomers. Before addition of Eu(fod)$_3$, the resonances of the methyl and methoxy peaks for both isomers were each accidentally degenerate; adding Eu(fod)$_3$ causes each of the nuclei to experience a different local magnetic field. The methyl peak of the least abundant isomer moves upfield and its methoxy peak moves downfield, while the more abundant isomer exhibits the opposite behavior. The relative amounts of the isomers can be obtained by integration of peaks.

The experimentally measured chemical shift $\delta_{\text{exp}}$ is a weighted average between the chemical shift $\delta$, in the free substrate and the chemical shift $\delta_{\text{LS}}$ in the lanthanide ion-substrate complex LS, the weighting factors being the respective molar fractions $X_s$ and $X_{\text{LS}}$:

$$\delta_{\text{exp}} = X_s\delta_s + X_{\text{LS}}\delta_{\text{LS}}, \text{ with } X_s + X_{\text{LS}} = 1$$

The two major factors that determine the probability of lanthanide interaction with a functional group are basicity and steric effects. A nearly linear correlation between basicity and induced shifts was found for the ortho and meta protons of para-substituted anilines. For a group of substituted phenols, the smallest shift was observed for the most acidic phenol, $p$-nitrophenol. The paramagnetic lanthanide ions which induce shifts are predominantly of a pseudocontact nature.$^{65,66}$ The inability to identify chemical shifts with the pseudocontact is one major problem in using LSR, since these shifts contain very important structural information which may be used in conformational studies.
Figure 7. Isomers of $p$-methoxy-$p'$-methylazoxybenzene and partial NMR spectra of the isomeric mixture upfield and downfield induced by the addition of Eu(fod)$_3$.

Figure 8. Scale model Eu-azoxybenzene adduct.
In general, it is assumed that marked changes in the conformation of the nucleophile are not introduced by complexation with the shift reagent, but exception may occur. If the site of complexation is on a flexible part of the molecule, more caution must be exercised than if the complexation occurs on a rigid part. Different types of conformational problems have been approached. Comprehensive discussions of conformational studies with shift reagents have been given by Hofer. A preferred site of complexation usually exists within a functional group with more than one potential site of complexation. A study of the lactam and lupanine indicates that the carbonyl oxygen is the preferred coordination site. In N-methyl-N-isopropylthioformamide, the lanthanide is apparently complexed to the sulfur atom. There is a small possibility of contact contribution in shifts observed with Pr$^{3+}$ and Eu$^{3+}$ shift reagents. The contribution is between 5% for Pr and 20% Eu$^{1+}$. The contact interaction and pseudocontact interaction are based on the formation of a complex between the substrate and the paramagnetic lanthanide shift reagent. Both contact and pseudocontact interaction seem to be inversely proportional to temperature. Therefore, the lanthanide induced shift increases at lower temperatures. Another consequence of lowering temperature is line broadening. An equilibrium can be considered to exist in the solution between the substrate S and the lanthanide shift reagent L.

\[ \text{LSR} + \text{S} \rightleftharpoons \text{LSR} \cdot \text{S} \]

This coordination is a rapid reversible equilibrium which can not be distinguished on the NMR time scale. The resulting spectrum in the presence of the LSR is a time average of its spectrum in the complexed and uncomplexed form. The more LSR added, the greater contribution from LSR$\cdot$S can be observed, resulting in a greater LIS. The LSR containing
shifts when it interacts with a hard-base such as oxygen-ether or thio-ether (which has a positive charge on sulfur).\textsuperscript{70} Side reactions may also occur that need to be considered. These include further complexation with the substrate and complexation of the shift reagent with itself.\textsuperscript{62}

\[ \text{LSR}\cdot S + S \rightleftharpoons \text{LSR}\cdot S_2 \]

\[ \text{LSR} + \text{LSR} \rightleftharpoons (\text{LSR})_2 \]

The rate of substrate exchange between free and coordinated forms is also rapid on the NMR time scale. Because both of these equilibria are rapid on the NMR time scale, the resonances observed for a substrate in the presence of these shift reagents is probably a time averaged result of at least three species.

**E. Lanthanide-Induced Chemical Shifts of Sulfonium Salts**

1. **Structural elucidation of sulfonium ions:** The use of lanthanide shift reagents (LSR) as tools in the structural elucidation of organosulfur compounds is well documented.\textsuperscript{71} These reagents have routinely been used in the analysis of numerous tricoordinate sulfur(IV) species such as sulfoxides and sulfilimines.

In 1980 Caret and Vennos used LSR in the investigation of the structure of sulfonium salts.\textsuperscript{72} Sulfonium salts give observable induced shifts when LSR's are employed. Also, these salts are more strongly shifted by the LSR than are the corresponding neutral sulfides. The closer the observed proton is to the site of complexation, the greater the induced shift. The origin of these shifts is primarily attributed to a pseudocontact interaction between the paramagnetic lanthanide shift reagent and the molecule being investigated.\textsuperscript{73} In the case of
the sulfonium salts, two sites of complexation are possible, the electron pair on sulfur and/or the anion (Figure 9).

![Figure 9. Two possible sites of sulfonium salt in complexation with LSR.](image)

To gain insight into the origin of this complexation, the 1,2-dimethyl-2,3-dihydrobenzothiophenium tetrafluoroborate system is adopted (Figure 10). The cis and trans isomers of the system had been synthesized and their configuration assigned previously. The cis/trans isomerism present in Figure 10 provides a convenient “way” for determining the site of complexation between the salt and the shift reagent.

![Figure 10. The cis and trans isomers of 1,2-dimethyl-2,3-dihydrobenzothiophenium.](image)
The salient geometric features of the two isomers are summarized in Figure 11. Note the position of the anion with respect to the methyl groups in each isomer. From X-ray data of analogous cyclic sulfonium salts, the anion would be predicted to be oriented in an area roughly in the plane of the thiophene ring as close to the positively sulfur as is sterically allowable. In addition, the negatively charged anion would remain oriented as far away as possible from the π-electron cloud of the aromatic ring and the electron pair on sulfur. If the lone pair is the site of complexation, then the SCH₃ of both the cis and trans isomers would be approximately equi-distant from the LSR, but the CCH₃ of the trans isomer would be much closer to the praseodymium than would the CCH₃ of the cis isomer. There should be a large difference in shift between these latter two methyl groups. The results of the LIS study on Figure 10 are given in Figure 12. These results are consistent with a complexation at or with the anion and not with the lone pair on sulfur. They also concluded that the magnitude of LIS is proportional to the size of anion. The greater LIS for bulkier anions such as FSO₃⁻ compared to BF₄⁻ was observed.

2. Racemization of chiral sulfonium ions: Optically active tertiary sulfonium salts have been known for many years, and there has been considerable interest in the mechanism of their racemization. This thermal racemization of optically active sulfonium salts may proceed by three routes: pyramidal inversion (A), dissociation by S_N1 mechanism (B), or dissociation by a S_N2(C) mechanism:
Figure 11. Geometric features in the two isomers of 1,2-dimethyl-2,3-dihydrobenzo-thiophenium
Figure 12. The LIS study of 1,2-dimethyl-2,3-dihydrobenzothiophenium tetrafluoroborate. The SCH₃ and CCH₃ resonances are plotted as a function of the ratio of shift reagent, Pr(tfc)₃, to substrate in CD₂Cl₂. Note that only methyl resonances are plotted for clarity.
Pathway C has been proposed for the racemization of optical active phenacyethylmethylsulfonylum iodide, and A has been described as "major pathway" for the racemization of t-buty lethylmethylsulfonylum perchlorate.\textsuperscript{83} t-buty lethylmethylsulfonylum perchlorate racemizes ca. 15-fold faster than it solvolyses in a variety of solvents, and it has been argued that racemization in ethanol occurs by pyramidal inversion about the central sulfur atom:

\[
R^1\\ \downarrow \quad S^1\\ \downarrow R^2 \quad \rightarrow \quad S^2 \quad \downarrow R^3
\]

An alternative mechanism, whereby heterolytic carbon-sulfur bond cleavage (4) yields a t-buty l cation-ethyl methyl sulfide ion-molecule pair (which may either return to racemic sulfonium salt or react with the solvent), is supported by measurements of activation volume\textsuperscript{82} ($\Delta V = +6.4 \text{ ml mol}^{-1}$) in water at 40 °C but has been ruled out for reaction in ethanol on the basis of substituent effects\textsuperscript{82}; thus, although the relative rates of ethanolysis (1:0.06:6.3) of 1:2:3 are consistent with a mechanism of heterolytic cleavage (under the influence of electron-withdrawing 2 or electron-donating 3 substituents), the relative rates of racemization (1:1.7:3.8) can best be attributed to increase in non-bonded interaction in the ground state, relative to the transition state, of a concerted pyramidal inversion:

\[
\begin{align*}
\text{Me} & \quad \text{Me} \\
\text{Me} & \quad \text{Me} \\
\text{Me} & \quad \text{Me} \\
\text{Me} & \quad \text{Me} \\
\text{Me} & \quad \text{Me} \\
\text{Me} & \quad \text{Me} \\
\text{Me} & \quad \text{Me} \\
\text{Me} & \quad \text{Me} \\
\text{Me} & \quad \text{Me} \\
\text{Me} & \quad \text{Me} \\
\text{Me} & \quad \text{Me} \\
\end{align*}
\]

1 \quad 2 \quad 3
Likewise, racemization of optically active 1-adamantylethylmethylsulfonium perchlorate in acetic acid is believed to occur by pyramidal inversion since no evidence for C-S bond heterolysis has been found; this salt fails to solvolyse under the racemization conditions and perchlorate ion is unlikely to promote inversion by a displacement mechanism, such as that proposed to account for racemization of l-phenacylethylmethylsulfonium halides:  

\[
\begin{align*}
S + X^- & \rightarrow S^- + n^3X \\
& \rightarrow X^- + n^3S_n^1
\end{align*}
\]

Although inversion mechanism is also believed to account for racemization of benzylethyl methyl-, p-nitrobenzylethyl-, and phenacylethylmethylsulfonium perchlorates (\(\Delta V^* \approx 0\) for reaction in \(H_2O, MeOH,\) and \(EtOH\) at 60 °C), there is evidence to suggest that \(p\)-methoxybenzylethylmethyl system 4 racemizes principally by C-S bond heterolysis:  

\[
\text{MeO} \quad \text{Cl}_2 \quad \text{MeO} \quad \text{Et} \quad \text{S}_{n^1} \quad \text{Me}_{n^3} \text{Et} \quad \text{Cl}_2 \quad \text{OMe}
\]

High ring strain during pyramidal inversion is believed to account for the slow rates of racemization of the cyclic sulfonium salts 5-7.  

Enantiomers of triarylsulfonium ions can
be isolated only if their unusually rapid pyramidal inversion is precluded by ring strain effects as in 8 or 9.\textsuperscript{85}

\begin{center}
\begin{tabular}{ccc}
5. & 6. & 7. \\
\end{tabular}
\end{center}

\begin{center}
8. & 9. \\
\end{center}

The racemization of optically active sulfonium and other "onium" salts should be a useful procedure for detecting bond heterolysis whenever this reaction is faster than all other processes which can result in racemization. For the sulfonium salts the formation of racemic starting material will require a simple rotation of the sulfide molecule relative to the carbonium ion within the solvent cage. The degree of rotation will depend on the detailed hybridization of the sulfide. The rotation will not require any further separation of the caged groups and should be energetically very facile.\textsuperscript{86}

Mislow and co-workers have suggested that many of sulfoxide systems also undergo racemization by a pyramidal inversion mechanism.\textsuperscript{87}
3. Resolution and Analysis of Chiral sulfonium ions by Lanthanide Shift Reagents: In 1987 Wenzel and Zaia reported the use of NMR lanthanide shift reagents for the analysis of sulfonium and isothiouronium salts (Scheme 1). For example, they found that when the europate complex Eu(fod)$_3$ is reacted with Kfod in the presence of a sulfonium tetrafluoroborate, ion pair formation occurs between the sulfonium cation and the tetrakis europate anion, Eu(fod)$_4$$. Precipitation of potassium fluoroborate drives the reaction toward ion-pair formation. This shift reagent interacts with the sulfonium ion to cause a dispersion of the peaks in the spectrum.

\[
\begin{align*}
R^- \cdot S^+ \cdot R'BF_4^- + Eu(fod)_3 + Kfod & \rightarrow R'' \cdot S^+ \cdot R'Eu(fod)_4^- + KBF_4^+ \\
R'' & 
\end{align*}
\]

Scheme 1.

The lanthanide ions that have now become generally adopted for practical use are the trivalent paramagnetic ions of europium, Eu$^{3+}$, praseodymium, Pr$^{3+}$, and ytterbium, Yb$^{3+}$. So that they can be dissolved in organic solvents, these ions are used in the form of complexes. The complexing agents most commonly used to make these chelates are the anions of the 1,1,2,2,3,3-heptfluoro-7,7-dimethyl-4,6-octandione (FOD), as the achiral reagent and tris [3-(2,2,2-trifluoro-1-hydroxyethylidene)-d-camphorato] (TFC) as the chiral agents.

F. Goal of This Study.

This research is aimed at developing NMR shift reagents for assessment of enantiomeric purity and resolution of chiral methyl sulfonium ions which can be used as a chiral alkylating agents in asymmetric syntheses. Praseodymium(III) NMR shift reagent,
which is an upfield shift reagent, is focused on for this research. For this purposes, concentration and temperature dependence of the chemical shift was also investigated.
II. EXPERIMENTAL SECTION.

A. Reagents.

Iodoctane, iodobutane, benzylbromide, methyl iodide, ethylphenyl sulfide, and thioanisole were purchased from Aldrich Chemical Company and were used without further purification. Silver tetrafluoroborate, Eu(tfc)$_3$, Eu(hfc)$_3$, Pr(tfc)$_3$, Pr(hfc)$_3$, H(fod), H(tfc), and H(hfc) were obtained from Aldrich Chemical Company and stored under an atmosphere of dry N$_2$ to prevent absorption of water in the atmosphere.

d$_2$-Methyl iodide was purchased from Aldrich Chemical Company and stored in the refrigerator. Potassium hydroxide was provided by the J. T. Baker Chemical Company. The chloroform-$d$ (99.8 atom %D) was purchased from Isotec Inc. and stored in a vessel with molecular sieves. 1,2-dichloroethane and acetonitrile were obtained from Aldrich Chemical Company. Anhydrous ethyl ether was purchased from EM Science.

B. Preparation of Sulfonium Salts.

A procedure similar to that of Acheson and Harrison was employed in the preparation of all sulfonium salts.$^{88}$

1. Ethylmethylphenylsulfonium tetrafluoroborate. (Scheme 2)- 1 mmol of ethyl phenyl sulfide and methyl iodide were dissolved in 2 ml of 1,2-dichloroethane (DCE). Adding 1.2 mmol of AgBF$_4$ which was prepared in 1 ml of DCE in N$_2$ atmosphere to the stirred solution caused the formation of AgI as a yellow precipitate. The reaction was allowed to
stir overnight. The solution was centrifuged and the precipitate was washed with DCE. Then the supernatant was transferred to a round-bottom flask and was rotary vaporized under 35 °C to remove solvent. The remaining oily product was vacuum-dried for 24 hours at room temperature. The final product was 0.28 g (90 %)

2. Ethyl-$d_2$-methylphenylsulfonyl tetrafluoroborate. (Scheme 2)- This sulfonium salt was prepared by reacting $d_2$-methyl iodide (1 mmol) with ethyl methyl sulfide (1 mmol) in the presence of silver tetrafluoroborate (1.2 mmol) in DCE (2 ml). AgI precipitate was removed and solvent was removed by rotary vaporization. After drying in a vacuum oven at room temperature, the oily product could be obtained.

R and S mixture.

Scheme 2.
3. **Butylmethylphenylsulfonium tetrafluoroborate. (Scheme 3)**- This sulfonium salt was prepared by reacting iodobutane (1 mmol) with thioanisole (1 mmol) in the presence of silver tetrafluoroborate (1.2 mmol) in DCE (2 ml). AgI precipitate was removed and solvent was removed by rotary vaporization. After drying in a vacuum oven at room temperature, the oil product could be obtained with 85% yield (0.224 g).

![Scheme 3](image)

R and S mixture.

4. **Methyloctylphenylsulfonium tetrafluoroborate. (Scheme 4)**- This sulfonium salt was prepared by reacting iodoctane (1 mmol) with thioanisole (1 mmol) in the presence of silver tetrafluoroborate (1.2 mmol) in DCE (2 ml). AgI precipitate was removed and solvent was removed by rotary vaporization. After drying in a vacuum oven at room temperature, the oil product could be obtained with 89% yield (0.35 g).
Scheme 4.

5. Benzylmethylphenylsulfonium tetrafluoroborate. (Scheme 5)-This sulfonium salt was prepared by reacting benzylbromide (1 mmol) with thioanisole (1 mmol) in the presence of silver tetrafluoroborate (1.2 mmol) in DCE (2 ml). AgI precipitate was removed and the solvent was removed by rotary vaporization. It was triturated with sufficient anhydrous diethyl ether so that the product was crystallized. After drying in a vacuum oven at room temperature, the solid product could be obtained with 80 % yield (0.24 g).

Scheme 5.
C. Formation of tetrakis Lanthanide anion-Sulfonium Pair. - A procedure established by Wenzel and Zaia was employed in the formation of tetrakis Lanthanide anion-sulfonium cation pair.39

1. Formation of tetrakis Praseodymium anion-Ethylmethylphenylsulfonium cation pair: The ethylmethylphenylsulfonium tetrafluoroborate (0.1 mmol), Pr(tfc)$_3$ (0.1 mmol), and K(tfc) (0.1 mmol) or K(fod) (0.1 mmol) were added to 4 ml canonical vial in 1ml of dry $d$-chloroform in a dry box. The mixture was magnetically stirred for 30 mins. The solution was centrifuged and the precipitate was removed. The supernatant was pipetted into an NMR tube.

To study the effect of concentration for shifting and dispersion of peaks, the supernatant with an initial concentration of 0.1 M was diluted to 0.05 M, 0.025 M. This salt was also stirred with Pr(hfc)$_3$ and K(hfc) under same experimental conditions.

To assign the methyl peak which is directly bonded to sulfur (S-methyl) in the shifted spectrum of ethylmethylphenylsulfonium salt, the ethyl-$d$_$_2$-methylphenylsulfonium salt and the normal ethylmethylphenylsulfonium salt were reacted with 0.1, 0.2, and 0.3 equivalents of Pr(tfc)$_3$ and K(tfc) with respect to the sulfonium salt, respectively. These 6 experiments were carried out under same experimental conditions, and the same work-up methods were employed for each reaction.

2. Formation of tetrakis Europium anion-Ethylmethylphenylsulfonium cation pair: The ethylmethylphenylsulfonium tetraborate (0.1 mmol) was stirred with Eu(hfc)$_3$ (0.1 mmol) and K(hfc) (0.1 mmol) under same experimental conditions, and same work-up methods were employed as above.
3. Formation of tetrakis Praseodymium anion-Butylmethylphenylsulfonium cation pair: The butylmethylphenylsulfonium tetrafluoroborate (0.1 mmol), Pr(tfc)$_3$ (0.1 mmol), and K(tfc) (0.1 mmol) or K(fod) (0.1 mmol) were added to 4 ml canonical vial in 1ml of dry $d$-chloroform in a dry box. The mixture was magnetically stirred for 30 mins. The solution was centrifuged and the precipitate was removed. The supernatant was pipetted into an NMR tube.

To study the effect of concentration for shifting and dispersion of peaks, the supernatant with an initial concentration of 0.1 M was diluted to 0.05 M, 0.025 M.

4. Formation of tetrakis Europium anion-Butylmethylphenylsulfonium cation pair: The butylmethylphenylsulfonium tetrafluoroborate was stirred with Eu(fod)$_3$ and K(fod), also with Eu(tfc)$_3$ and K(fod) under same experimental conditions.

5. Formation of tetrakis Praseodymium anion-Methyloctylphenylsulfonium cation pair: The methyloctylphenylsulfonium tetrafluoroborate (0.1 mmol), Pr(tfc)$_3$ (0.1 mmol), and K(tfc) (0.1 mmol) or K(fod) (0.1 mmol) were added to 4 ml canonical vial in 1ml of dry $d$-chloroform in a dry box. The mixture was magnetically stirred for 30 mins. The solution was centrifuged and the precipitate was removed. The supernatant was pipetted into an NMR tube.

To study the effect of concentration for shifting and dispersion of peaks, the supernatant with an initial concentration of 0.1 M was diluted to 0.05 M, 0.025 M. This sulfonium salt was also stirred with Pr(hfc)$_3$ and K(hfc) under same experimental conditions.
In order to track the movement of peaks in methyloctylphenylsulfonium spectrum shifted by Pr(hfc)$_2$, the sulfonium salt was stirred with 0.2, 0.4, 0.6, and 0.7 equivalents of Pr(hfc)$_3$ and K(hfc), relative to the sulfonium salt.

6. Formation of tetrakis Europium anion-Methylcetylphenylsulfonium cation pair: This sulfonium salt was stirred with Eu(hfc)$_3$ and K(hfc), Eu(tfc)$_3$ and K(tfc), Eu(fod)$_3$ and K(fod), Eu(tfc)$_3$ and K(fod) under same experimental conditions as above.

7. Formation of tetrakis Praseodymium anion-Benzylmethylphenyl sulfonium cation pair: The benzylmethylphenylsulfonium tetrafluoroborate (0.1 mmol), Pr(tfc)$_3$ (0.1 mmol), and K(tfc) (0.1 mmol) or K(fod) (0.1 mmol) were added to 4 ml canonical vial in 1mL of dry $d$-chloroform in a dry box. The mixture was magnetically stirred for 30 mins. The solution was centrifuged and the precipitate was removed. The supernatant was pipetted into a NMR tube.

To study the effect of concentration for shifting and dispersion of peaks, the supernatant with an initial concentration of 0.1 M was diluted to 0.05 M, 0.025 M.

8. Formation of tetrakis praseodymium anion-R-enriched-ethylmethyl-p-tolylsulfonium cation pair: This salt (0.5 mmol) was stirred with Pr(tfc)$_3$ (0.5 mmol) and K(tfc) (0.5 mmol) under same experimental conditions as above.

D. Preparation of K(fod), K(tfc), and K(hfc).

1 mmol of H(fod), H(tfc), or H(hfc) was treated with 2 ml of 50 % aqueous solution of KOH, respectively. The white solid of K(fod) and K(tfc) and yellow solid of K(hfc) immediately formed and was filtered and washed with 1 mL cold water. The product was dried for 24 hours in vacuum oven at room temperature.
E. NMR characterization of sulfonium salts.

The \(^1\)H NMR spectra were recorded by JEOL CPF 270 FT-NMR. Two kinds of NMR experimental conditions were adopted (Table III).

<table>
<thead>
<tr>
<th></th>
<th>Unshifted Spectra</th>
<th>Shifted Spectra</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spectra Width</td>
<td>5405.4 Hz.</td>
<td>20000.00 Hz.</td>
</tr>
<tr>
<td>Number of Pulse</td>
<td>32</td>
<td>64</td>
</tr>
<tr>
<td>Pulse Delay</td>
<td>1.000 sec.</td>
<td>1.000 sec.</td>
</tr>
<tr>
<td>Pulse Width</td>
<td>5.2 sec.</td>
<td>5.2 sec.</td>
</tr>
<tr>
<td>Acquisition Time</td>
<td>1.516 sec.</td>
<td>0.410 sec.</td>
</tr>
</tbody>
</table>
III. RESULTS AND DISCUSSIONS.

A. Syntheses of sulfonium salts.

A series of alkylmethylphenyl sulfonium salts were synthesized, where alkyl is ethyl, butyl, octyl, and benzyl, with over 85 % yield. These salts could be used without further purification. Only benzylmethylphenyl sulfonium tetrafluoroborate was white solid, and the other three salts were pale yellow, oily compounds. These salts were stored in a dessicator to prevent absorption of moisture in air.

B. Ethylmethylphenyl sulfonium ion.

1. Ethylmethylphenylsulfonium tetrafluoroborate: The $^1$H NMR spectrum of this sulfonium salt in $d_6$-acetone is shown in Figure 13. The methyl peaks which are directly bonded to sulfur (S-methyl) are observed at 3.5 ppm. The other methyl resonance appears at 1.4 ppm. The diastereotopic methylene resonances can be seen at 3.9 ppm. Ortho hydrogen resonances are exhibited at 8.2 ppm, and para/meta peaks are seen at 7.7-7.8 ppm.

Ethyl-$d_7$-methylphenylsulfonium tetrafluoroborate (Figure 14) exhibits the same chemical shifts except that the S-methyl resonance is absent, as expected.

2. Formation of tetrakis lanthanide anion-ethylmethylphenylsulfonium cation pair.

a. Tetrakis praseodymium anion-ethylmethylphenylsulfonium cation pair.: We investigated three kinds of praseodymium anions for this sulfonium salt; Pr(tfc)$_4^-$, Pr(tfc)$_3$fod$^-$, and Pr(hfc)$_4^-$.
Figure 13: The $^1H$ NMR spectrum of ethylphenylphenyldiisourea in $d_6$-acetone.
Figure 14  The $^1$H NMR spectrum of ethyl-$d_3$-methylphenylsulfonium tetrafluoroborate in $d_6$-acetone.
Ion Pair Formation with Pr(tfc)₄⁻

Effect of Temperature: A 0.1 M solution of the ethylmethylphenylsulfonium cation-Pr(tfc)₄⁻ anion was prepared in d-chloroform. ¹H NMR spectra were obtained at 20, 30, 40, and -10 °C as shown in Figures 15-18. The S-methyl and diastereotopic methylene resonances are strongly shifted upfield to between -20- -30 ppm and appear as very broad resonances. These signals are not shown in the Figures 15-17.

The best enantiomeric resolution, as shown in Figure 15, was observed for the ortho hydrogen resonances, which are nearly baseline resolved at about -3 ppm. The methyl resonances of the ethyl group were also resolved at -8 ppm. The meta and para hydrogen resonances are also distinguished but not enantiomerically resolved. The best overall result was obtained at -10 °C, as shown in Figure 18. In this spectrum all resonances of this sulfonium ion are enantiomerically resolved, including even the para and meta hydrogen resonances. The effect of raising temperature is to shift the signals downfield, as shown in Figures 16 and 17. Apparently, at lower temperature, the ion-pair interaction is greater, causing a larger change in chemical shift. The results are summarized in Table IV.

Table IV. ¹H NMR chemical shift of ethylmethylphenylsulfonium ion in the presence of Pr(tfc)₄⁻ as a function of temperature.

<table>
<thead>
<tr>
<th></th>
<th>Ortho Protons</th>
<th>Meta/Para Protons</th>
<th>S-methyl Protons</th>
<th>Methyl Protons in ethyl group.</th>
</tr>
</thead>
<tbody>
<tr>
<td>20 °C</td>
<td>-2.9 ppm</td>
<td>4.1/4.7 ppm</td>
<td>-27.5 ppm</td>
<td>-8.9 ppm</td>
</tr>
<tr>
<td>30 °C</td>
<td>-2.3 ppm</td>
<td>4.3/4.9 ppm</td>
<td>-26 ppm</td>
<td>-8 ppm</td>
</tr>
<tr>
<td>40 °C</td>
<td>-1.9 ppm</td>
<td>4.5/5 ppm</td>
<td>-25 ppm</td>
<td>-7.5 ppm</td>
</tr>
</tbody>
</table>
Figure 15. The $^1$H NMR spectrum of ethylmethylphenylsulfonium tetrakis-(tfc)$_4$ praseodymium (III) in CDCl$_3$ at 20 °C.
Figure 16. The $^1$H NMR spectrum of ethylmethylphenylsulfonium tetrakis-(tfc)$_4^-$ praseodymium (III) in CDCl$_3$ at 30 °C.
Figure 17. The $^1$H NMR spectrum of ethylmethylphenylsulfonium tetrakis-(tfc)$_4^-$ praseodymium (III) in CDCl$_3$ at 40 °C.
Figure 18. The $^1$H NMR spectrum of ethylmethylphenylsulfonium tetrakis-(tfc)$_4$ praseodymium (III) in CDCl$_3$ at -10 °C.
Effect of Concentration of Shift Reagent: The concentration of Pr(tfc)$_4$ anion was varied with constant 0.1 M concentration of ethylmethylphenylsulfonium ion. This experiment aided in making assignments of the various resonances. As expected, the resonances move upfield as concentration of shift reagent increases, as shown Figures 19-21, and these resonances can be “tracked” as they move with concentration. As shown in Figure 21, where the concentration of shift reagent is 0.03 M (0.3 equivalent shift reagent), two broad resonances are observed at -3 to -5 ppm. To make assignment, the spectrum of ethyl-$d_7$-methylphenyl sulfonium ion was obtained at the same concentration of shift reagent. This spectrum, as shown in Figure 22, shows the more intense, more upfield resonance to be absent, allowing assignment of this resonance to the S-methyl resonances.

Analysis of R-enriched Ethylmethyl-$p$-tolylsulfonium ion: In order to make assignment of the resonances associated with R and S isomers, the spectrum of the R-enriched ethylmethyl-$p$-tolylsulfonium ion in the presence of Pr(tfc)$_4$ was obtained. This R-enriched sulfonium ion was synthesized from (R)-methyl-$p$-tolylsulfoxide with diethylcadmium and trimethyloxomium tetrafluoroborate according to the standard literature synthesis. The spectrum was obtained at 0.05 M concentration of shift reagent and sulfonium ion and is shown in Figure 23. Assignments are made in the Figure.

Racemization of R-enriched Ethylmethyl-$p$-tolylsulfonium ion: Dialkylaryl sulfonium ions are known to undergo pyramidal inversion at significant rates near 50 °C. Therefore, the R-enriched ethylmethyl-$p$-tolylsulfonium cation-Pr(tfc)$_4$ ion pair was heated to 50°C in order to see if pyramidal inversion might be observed. The spectra were obtained
Figure 19. The $^1$H NMR spectrum of ethylmethylphenylsulphonium ion: 0.1 equivalent of Pr(tfc)$_4$ in CDCl$_3$. 
Figure 20. The $^1$H NMR spectrum of ethylmethylphenylsulfonium ion: 0.2 equivalent of Pr(tfc)$_4^-$ in CDCl$_3$. 
Figure 21. The $^1$H NMR spectrum of ethylmethylphenylsulfonium ion: 0.3 equivalent of Pr(tfc)$_4^-$ in CDCl$_3$.
Figure 22. The $^1$H NMR spectrum of ethyl-$d_3$-methylphenylsulfonium ion: 0.3 equivalent of Pr(tfc)$_4$ in CDCl$_3$. 
Figure 23. The $^1$H NMR spectrum of R-enriched-ethylmethyl-$p$-tolylsulfonium tetrakis-(tfc)$_4^-$ praseodymium(III) in CDCl$_3$ at 20 °C.
Figure 24. The $^1$H NMR spectrum of ortho protons of R-enriched-ethylmethyl-$p$-tolylsulfonium tetrakis-(tfc)$_4$ praseodymium(III) in CDCl$_3$. Initial heating at 50°C.
Figure 25. The $^1$H NMR spectrum of ortho protons of R-enriched-ethylmethyl-$p$-tolylsulfonium tetrakis-(tfc)$_4$ praseodymium(III) in CDCl$_3$. After 1 hour heating at 50°C.
Figure 26. The $^1$H NMR spectrum of ortho protons of R-enriched-ethylmethyl-p-tolylsulfonium tetrakis-(tfc)$_2$ praseodymium(III) in CDCl$_3$. After 11 hours heating at 50 °C.
at 0 hour, 1 hour, and 11 hours and are shown in Figures 24-26, where the ortho hydrogen resonances are expanded. Racemization is completed in 11 hours.

**Ion Pair formation with Pr(tfc)$_3$(fod):** A 0.1 M solution of the ethylmethylphenylsulfonium cation-Pr(tfc)$_3$(fod)$^-$ anion was prepared in $d$-chloroform. $^1$H NMR spectra were obtained at 20 and 30 °C, as shown in Figures 27-28. Ortho hydrogens are enantiomerically resolved about 4.3 ppm at 20 °C, but show no spin-spin splitting. The diastereotopic methylene resonances exhibit some resolution about -6 and -7.8 ppm at 20 °C. There is no significant resolution with Pr(tfc)$_3$(fod)$^-$ . The results are summarized in Table V.

**Table V.** $^1$H NMR chemical shift of ethylmethylphenylsulfonium ion in the presence of Pr(tfc)$_3$(fod)$^-$ as a function of temperature.

<table>
<thead>
<tr>
<th></th>
<th>Ortho Protons</th>
<th>Meta/Para Protons</th>
<th>S-methyl Protons</th>
<th>Diastereotopic methylene Protons</th>
</tr>
</thead>
<tbody>
<tr>
<td>20 °C</td>
<td>4.3 ppm</td>
<td>6.3/6.5 ppm</td>
<td>-6.8 ppm</td>
<td>-6/-7.8 ppm</td>
</tr>
<tr>
<td>30 °C</td>
<td>4.5 ppm</td>
<td>6.3/6.6 ppm</td>
<td>-6.5 ppm</td>
<td>-5.5/-7.3 ppm</td>
</tr>
</tbody>
</table>

**Ion Pair formation with Pr(hfc)$_4$:** A 0.1 M solution of the ethylmethylphenyl sulfonium cation-Pr(hfc)$_4$ anion was prepared in $d$-chloroform. $^1$H NMR spectra were obtained at 20, 30, 40 °C as shown in Figure 29-31. Methyl resonance in ethyl group are shown at -3.5 ppm with some resolution (Figure 29). The meta and para hydrogen resonances can be
Figure 27. The $^1$H NMR spectrum of ethylmethylphenylsulfonium tetrakis-(tfc)$_3$(fod)$^-$ praseodymium(III) in CDCl$_3$ at 20 °C.
Figure 28. The $^1$H NMR spectrum of ethylmethylphenylsulfonium tetrakis-(tfc)$_3$ (fod)$^-$ praseodymium(III) in CDCl$_3$ at 30 °C.
Figure 29. The $^1$H NMR spectrum of ethylmethylphenylsulfonium tetrakis-(hfc)$_4^+$ praseodymium (III) in CDCl$_3$ at 20 °C.
Figure 30. The $^1$H NMR spectrum of ethylmethylphenylsulfonylum tetrakis-(hfc)$_4^-$ praseodymium (III) in CDCl$_3$ at 30 °C.
Figure 31. The $^1$H NMR spectrum of ethylmethylphenylsulfonium tetrakis-(hfc)$_4$ praseodymium (III) in CDCl$_3$ at 40 °C.
distinguished but not enantiomerically resolved. In the case of ortho hydrogens there is no resolution. The results are summarized in Table VI.

**Table VI.** $^1$H NMR chemical shift of ethylmethylphenylsulfonium ion in the presence of $\text{Pr(hfc)}_4$ as a function of temperature.

<table>
<thead>
<tr>
<th></th>
<th>Ortho Protons</th>
<th>Meta/Parα Protons</th>
<th>Methyl protons in ethyl group</th>
</tr>
</thead>
<tbody>
<tr>
<td>20 °C</td>
<td>2 ppm</td>
<td>5.3/5.9 ppm</td>
<td>-3.5 ppm</td>
</tr>
<tr>
<td>30 °C</td>
<td>2.7 ppm</td>
<td>5.5/6 ppm</td>
<td>-3.3 ppm</td>
</tr>
<tr>
<td>40 °C</td>
<td>2.7 ppm</td>
<td>5.5/6 ppm</td>
<td>-3.2 ppm</td>
</tr>
</tbody>
</table>

**b. Tetrakis europium anion-ethylmethylphenyl sulfonium cation pair.** We investigated $\text{Eu(hfc)}_4^-$ as anion for this sulfonium salt. The europium complexes causes the shifts of signals to move down field, in contrast to praseodymium.

**Ion Pair formation with Eu(hfc)$_4^-$:** A 0.1 M solution of the ethylmethylphenyl sulfonium cation-Eu(hfc)$_4^-$ anion was prepared in $d$-chloroform. $^1$H NMR spectra were obtained at 20, 30, 40 °C as shown in Figures 32-34. There is no resolution except that one of the diastereotopic methylene resonances and the methyl resonance of the ethyl group show some resolution. The S-methyl peak can be observed at 18.3 ppm, and diastereotopic protons are exhibited at 15 ppm at 20 °C, it is observed that S-methyl peak moves dramatically from 18.4 to upfield about 14.5 ppm. The results are summarized in Table VII.
Figure 32. The $^1$H NMR spectrum of ethylmethylphenylsulfonium tetrakis-(hfc)$_4^-$ europium(III) in CDCl$_3$ at 20°C.
Figure 33. The $^1$H NMR spectrum of ethylmethylphenylsulphonium tetrakis-(hfc)$_4$ europium(III) in CDCl$_3$ at 30 °C.
Figure 34. The $^1$H NMR spectrum of ethylmethylphenylsulphonium tetrakis-(hfc)$_4$ europium(III) in CDCl$_3$ at 40 °C.
Table VII. $^1$H NMR chemical shift of ethylmethylphenylsulfonium ion in the presence of Eu(hfc)$_4^-$ as a function of temperature.

<table>
<thead>
<tr>
<th></th>
<th>Ortho Protons</th>
<th>Meta/Para Protons</th>
<th>Diastereotopic methylene Protons</th>
<th>S-methyl Protons</th>
<th>Methyl Protons in ethyl group</th>
</tr>
</thead>
<tbody>
<tr>
<td>20 °C</td>
<td>13.5 ppm</td>
<td>10/9.7 ppm</td>
<td>14-15.7 ppm</td>
<td>18.3 ppm</td>
<td>6 ppm</td>
</tr>
<tr>
<td>30 °C</td>
<td>13.2 ppm</td>
<td>9.8/9.7 ppm</td>
<td>13.2-13.7 ppm</td>
<td>15 ppm</td>
<td>5.8 ppm</td>
</tr>
<tr>
<td>40 °C</td>
<td>12.9 ppm</td>
<td>9.8/9.4 ppm</td>
<td>13-13.5 ppm</td>
<td>14.5 ppm</td>
<td>5.5 ppm</td>
</tr>
</tbody>
</table>

C. Butylmethylphenyl Sulfonium ion.

1. Butylmethylphenylsulfonium tetrafluoroborate: The $^1$H NMR spectrum of this sulfonium salt in $d_6$-acetone is shown in Figure 35. The methyl peaks which are directly bonded to sulfur (S-methyl) are observed at 3.5 ppm. The butyl resonance appears at 1.4-1.8 ppm. The diastereotopic methylene resonances can be seen at 3.9 ppm. Ortho hydrogen resonances are exhibited at 8.2 ppm, and the para/meta hydrogens are seen at 7.7-7.8 ppm.

2. Formation of tetrakis lanthanide anion-butylmethylphenylsulfonium cation pair.

a. Tetrakis praseodymium anion-butylmethylphenylsulfonium cation pair: We investigated two kinds of praseodymium anions for this sulfonium salt: Pr(tfc)$_4^-$ and Pr(tfc)$_3$(fod)$^-$. 
Figure 35. The $^1$H NMR spectrum of butylmethylphenylsulfonium tetrafluoroborate in $d_6$-acetone.
**Ion Pair Formation with Pr(tfc)$_4^-$**: A 0.1 M solution of the butylmethylphenyl sulfonium cation-Pr(tfc)$_4^-$ anion was prepared in $d$-chloroform. $^1$H NMR spectra were obtained at 20 and 30 °C as shown in Figures 36-37. The ortho hydrogen resonances can be observed at 4 ppm with best resolution, and meta/para hydrogens are overlapped with ligand peaks around 6-7 ppm (Figure 36). The resonances which might be diastereotopic methylene protons and S-methyl signals are exhibited around -4.5 ppm and -8.5 ppm, respectively (Figure 36).

**Ion Pair Formation with Pr(tfc)$_3$(fod)$^-$**: A 0.1 M solution of the butylmethylphenyl sulfonium cation-Pr(tfc)$_3$(fod)$^-$ anion was prepared in $d$-chloroform. $^1$H NMR spectra were obtained at 20 and 30 °C as shown in Figure 38-39. This chiral shift reagent causes a great shift of the resonances compared to Pr(tfc)$_4^-$: The ortho hydrogen resonances are overlapped with ligand resonance and are not apparent. The S-methyl resonances are shown at -16 ppm with some resolution. The diastereotopic methylene protons can be observed at -8.5 ppm (Figure 38). The $\beta$-methylene resonance in the butyl group is a singlet at -6 ppm. Overall, good resolution cannot be obtained with this shift reagent.

**b. Tetrakis Europium anion-butylmethylphenylsulfonium cation pair**: We investigated Eu(tfc)$_3$(fod)$^-$ anions for this sulfonium salt.

**Ion Pair Formation with Eu(tfc)$_3$(fod)$^-$**: A 0.1 M solution of the butylmethylphenyl sulfonium cation-Eu(tfc)$_3$(fod)$^-$ anion was prepared in $d$-chloroform. $^1$H NMR spectra are obtained at 20 °C as shown in Figure 40. Ortho hydrogen resonances are exhibit the best resolution at about 14 ppm. S-methyl protons are observed at 27.5 ppm with no resolution.
Figure 36. The $^1$H NMR spectrum of butylmethylphenylsulfonium tetrakis-(tfc)$_4^-$ praseodymium (III) in CDCl$_3$ at 20 °C.
Figure 37. The $^1$H NMR spectrum of butylmethylphenylsulfonium tetrakis-(tfc)$_4^-$ praseodymium (III) in CDCl$_3$ at 30 °C.
Figure 38. The $^1$H NMR spectrum of butylmethylphenylsulfonium tetrakis-(tfc)$_3$ (fod)$^-$ praseodymium(III) in CDCl$_3$ at 20 °C.
Figure 39. The $^1$H NMR spectrum of butylmethylphenylsulfonium tetrakis-(tfc)$_3$ (fod)$^{-}$ praseodymium(III) in CDCl$_3$ at 30 °C.
Figure 40. The $^1$H NMR spectrum of butylmethylphenylsulfonyltrimethylammonium tetrakis-(tfc)$_3$ (fod)$^-$ europium (III) in CDCl$_3$ at 20 °C.
Around 17.5 ppm diastereotopic methylene resonances are shown. Overall, good resolution cannot be obtained, except for the ortho hydrogen signals.

D. Methyloctylphenylsulphonium ion.

1. Methyloctylphenylsulphonium tetrafluoroborate: The $^1$H NMR spectrum of this sulphonium salt in $d_6$-acetone is shown in Figure 41. The methyl peaks which are directly bonded to sulfur (S-methyl) are observed at 3.5 ppm. The methylene resonances appear at 1.2-1.9 ppm. The diastereotopic methylene resonance can be seen at 3.9 ppm. Ortho hydrogens are exhibited at 8.2 ppm, and the meta and para resonance are seen at 7.7-7.8 ppm.

2. Formation of tetrakis lanthanide anion-methyloctylphenylsulphonium cation pair.

a. Tetrakis praseodymium anion-methyloctylphenyl sulphonium cation pair: We investigated two kinds of praseodymium anions for this sulphonium salt: Pr(tfc)$_4^-$ and Pr(hfc)$_4^-$. Ion Pair Formation with Pr(tfc)$_4^-$. A 0.1 M solution of the methyloctylphenyl sulphonium cation-Pr(tfc)$_4^-$ anion was prepared in $d$-chloroform. $^1$H NMR spectra were obtained at 20, 30, and 40 ºC as shown in Figures 42-44. The spin-spin splitting of the aromatic hydrogens is retained. There are two well-resolved doublets for the ortho hydrogens. Two well-resolved triplets for the meta and para protons are exhibited about 6.5-6.7 ppm, and are expanded. (Figure 42). As expected, when the temperature increases these aromatic resonances move downfield and the meta and para protons are overlapped with ligand peaks. Diastereotopic methylene protons show some resolution, and as the temperature increases these protons are overlapped with ligand peaks as shown in Figure 44.
Figure 41. The $^1$H NMR spectrum of methyloctylphenylsulfonium tetrafluoroborate in $d_6$-acetone.
Figure 42. The $^1$H NMR spectrum of methyloctylphenylsulfonium tetrakis-(tfc)$_4$' praesodymium (III) in CDCl$_3$ at 20 °C.
Figure 37. The $^1$H NMR spectrum of methyloctylphenylsulfonium tetrakis-(tfc)$_4$ praseodymium (III) in CDCl$_3$ at 30 °C.
Figure 37. The $^1$H NMR spectrum of butylmethylphenylsulfonium tetrakis-(tfc)$_4^-$ praseodymium (III) in CDCl$_3$ at 30 °C.

Figure 44. The $^1$H NMR spectrum of methyloctylphenylsulfonium tetrakis-(tfc)$_4^-$ praseodymium (III) in CDCl$_3$ at 40 °C.
S-methyl resonances are exhibited in two well resolved singlets. The methylene resonances in the octyl group are overlapped with ligand peaks around -1.5~1 ppm. Temperature variation allows us to track the movement of the \( \beta \)-methylene resonance in the octyl group. The results are summarized in Table VIII.

Table VIII. \( ^1H \) NMR chemical shift of methyloctylphenylsulfonium ion in the presence of \( \text{Pr(tfc)}_4 \) as a function of temperature.

<table>
<thead>
<tr>
<th></th>
<th>Ortho Protons</th>
<th>Meta/Para Protons</th>
<th>S-methyl Protons</th>
<th>Diastereotopic methylene Protons</th>
<th>( \beta )-methylene resonance in octyl group</th>
</tr>
</thead>
<tbody>
<tr>
<td>20 °C</td>
<td>4.7 ppm</td>
<td>6.6/6.8 ppm</td>
<td>-6 ppm</td>
<td>-3 ppm</td>
<td>-1.3 ppm</td>
</tr>
<tr>
<td>30 °C</td>
<td>4.8 ppm</td>
<td>6.7/7 ppm</td>
<td>-5.9 ppm</td>
<td>-2.7 ppm</td>
<td>-0.8 ppm</td>
</tr>
<tr>
<td>40 °C</td>
<td>5 ppm</td>
<td>6.8/7 ppm</td>
<td>-5.7 ppm</td>
<td>-2.5 ppm</td>
<td>-0.5 ppm</td>
</tr>
</tbody>
</table>

**Ion formation with \( \text{Pr(hfc)}_4 \)**

**Effect of Temperature:** A 0.1 M solution of the methyloctylphenylsulfonium cation-\( \text{Pr(hfc)}_4 \) anion was prepared in \( \alpha \)-chloroform. \( ^1H \) NMR spectra were obtained at 20, 30, and 40 °C as shown in Figures 45-47. The resonance of the various methylene protons can be distinguished by variation of temperature, but there is no enantiomeric resolution. Also, temperature changes do not give any advantage for assigning ortho hydrogens which are overlapped with ligand peaks. The results are summarized in Table IX.
Figure 45. The $^1$H NMR spectrum of methyloctylphenylsulfonium tetrakis-(hfc)$_4^-$ praseodymium (III) in CDCl$_3$ at 20 $^\circ$C.
Figure 46. The $^1$H NMR spectrum of methyloctylphenylsulphonium tetrakis-(hfc)$_4^-$ praseodymium (III) in CDCl$_3$ at 30 °C.
Figure 47. The $^1$H NMR spectrum of methyloctylphenylsulfonium tetrakis-(hfc)$_4$ praseodymium (III) in CDCl$_3$ at 40 °C.
Table IX. $^1$H NMR chemical shift of methyloctylphenylsulfonium ion in the presence of Pr(tfc)$_4$ as a function of temperature.

<table>
<thead>
<tr>
<th></th>
<th>Meta/Para Protons</th>
<th>Diastereotopic methylene protons</th>
<th>S-methyl Protons</th>
<th>2nd methylene Protons in octyl group</th>
</tr>
</thead>
<tbody>
<tr>
<td>20 °C</td>
<td>4.9/5.5 ppm</td>
<td>-3.9 ppm</td>
<td>-11 ppm</td>
<td>-2 ppm</td>
</tr>
<tr>
<td>30 °C</td>
<td>5/5.6 ppm</td>
<td>-3.5 ppm</td>
<td>-8.8 ppm</td>
<td>-1.9 ppm</td>
</tr>
<tr>
<td>40 °C</td>
<td>5.1/5.8 ppm</td>
<td>-3.2 ppm</td>
<td>-6.2 ppm</td>
<td>-1.8 ppm</td>
</tr>
</tbody>
</table>

**Effect of Concentration of Shift Reagent:** The concentration of Pr(hfc)$_4$ anion was varied with constant 0.1 M concentration of sulfonium ion. This experiment could allow us to make assignments of various methylene resonances in the octyl group. As expected, the resonances of the sulfonium ion move upfield as the concentration of the shift reagent increases, as shown in Figure 48-51. As shown in Figure 48, where the concentration of shift reagent is 0.02 M (0.2 equivalent shift reagent), overlapping methylene resonances are observed at 0~1 ppm. It is observed that these overlapping methylene signals are spread out upfield when the shift reagent concentration progressively increases. This gradual increase of shift reagent concentration allows us to assign almost all methylene resonances in the octyl group.

b. **Tetrakis europium anion-methyloctylphenylsulfonium cation pair:** We investigated three kinds of praseodymium anions for this sulfonium salt: Eu(tfc)$_4$-, Eu(hfc)$_4$-, and Eu(tfc)$_3$(fod)$^-$.
Figure 48. The $^1$H NMR spectrum of methyloctylphenylsulfonium ion: 0.2 equivalent of Pr(hfc)$_4^-$ in CDCl$_3$, at 20 °C.
Figure 49. The $^1$H NMR spectrum of methyloctylphenylsulfonium ion: 0.4 equivalent of Pr(hfc)$_4^-$ in CDCl$_3$ at 20 °C.
Figure 50. The $^1$H NMR spectrum of methylloctylphenylsulfonylum ion: 0.6 equivalent of Pr(hfc)$_4^{-}$ in CDCl$_3$ at 20 °C.
Figure 51. The $^1$H NMR spectrum of methylloctylphenylsulfonium ion: 0.7 equivalent of Pr(hfc)$_4^-$ in CDCl$_3$ at 20 °C.
Figure 52. The $^1$H NMR spectrum of methylcyclohexylphenylsulfonium tetrakis-(tfc)$_4^-$ europium (III) in CDCl$_3$ at 20 °C.
Figure 53. The $^1$H NMR spectrum of methyl-octylphenylsulfonium tetrakis-(tfc)$_4^-$ europium(III) in CDCl$_3$ at 30 °C.
Figure 54. The $^1$H NMR spectrum of methyloctylphenylsulfonium tetrakis-(tfc)$_4^-$ europium (III) in CDCl$_3$ at 40 °C.
**Ion Pair Formation with Eu(tfc)$_4$**: A 0.1 M solution of the methyloctyiphenylsulfonium cation-Eu(tfc)$_4$ anion was prepared in $d$-chloroform. $^1$H NMR spectra were obtained at 20, 30, and 40 °C as shown in Figure 52-54. Ortho hydrogen resonances are enantiomerically resolved. S-methyl resonances, diastereotopic methylene protons, and meta/para protons are distinguished but not enantiomerically resolved. The results are summarized in Table X.

**Table X. $^1$H NMR chemical shift of methyloctyiphenylsulfonium ion in the presence of Eu(tfc)$_4$ as function of temperature.**

<table>
<thead>
<tr>
<th>Temperature</th>
<th>Ortho Protons</th>
<th>Meta/Para Protons</th>
<th>S-methyl Protons</th>
<th>Diastereotopic methylene Protons</th>
</tr>
</thead>
<tbody>
<tr>
<td>20 °C</td>
<td>12.6 ppm</td>
<td>9 ppm</td>
<td>21 ppm</td>
<td>14.5 ppm</td>
</tr>
<tr>
<td>30 °C</td>
<td>12.4 ppm</td>
<td>8.7 ppm</td>
<td>20 ppm</td>
<td>14 ppm</td>
</tr>
<tr>
<td>40 °C</td>
<td>12.2 ppm</td>
<td>8.7 ppm</td>
<td>19 ppm</td>
<td>13.5 ppm</td>
</tr>
</tbody>
</table>

**Ion Pair Formation with Eu(hfc)$_4$**: A 0.1 M solution of the methyloctyiphenylsulfonium cation-Eu(hfc)$_4$ anion was prepared in $d$-chloroform. $^1$H NMR spectra were obtained at 20, 30, and 40 °C as shown in Figures 55-57. There is no enantiomeric resolution of the ortho hydrogen resonances. As temperature increases the diastereotopic methylene resonances exhibit some resolution (Figures 56, 57). Resolution of S-methyl protons are observed at 40 °C (Figure 57). The results are summarized in Table XI.
Figure 55. The $^1$H NMR spectrum of methyl octylphenylsulphonium tetrakis-(hfc)$_4^-$ europium (III) in CDCl$_3$ at 20 °C.
Figure 56. The $^1$H NMR spectrum of methyloctylphenylsulfonium tetrakis-(hfc)$_4$ europium (III) in CDCl$_3$ at 30 °C.
Figure 57. The $^1$H NMR spectrum of methyloctylphenylsulfonium tetrakis-(hfc)$_4$ europium (III) in CDCl$_3$ at 40 °C.
Table XI. $^1$H NMR chemical shift of methyloctyiphenylsulfonium ion in the presence of Eu(hfc)$_4$ as function of temperature.

<table>
<thead>
<tr>
<th></th>
<th>Ortho Protons</th>
<th>Meta/Para Protons</th>
<th>S-methyl Protons</th>
<th>Diastereotopic methylene Protons</th>
</tr>
</thead>
<tbody>
<tr>
<td>20 °C</td>
<td>14 ppm</td>
<td>10.2/9.7 ppm</td>
<td>21 ppm</td>
<td>12.5 ppm</td>
</tr>
<tr>
<td>30 °C</td>
<td>13.5 ppm</td>
<td>10/9.6 ppm</td>
<td>17 ppm</td>
<td>11.8 ppm</td>
</tr>
<tr>
<td>40 °C</td>
<td>13.2 ppm</td>
<td>9.8/9.5 ppm</td>
<td>13.8 ppm</td>
<td>11.2 ppm</td>
</tr>
</tbody>
</table>

**Ion Pair Formation with Eu(tfc)$_3$(fod):** A 0.1 M solution of the methyloctyiphenylsulfonium cation-Eu(tfc)$_3$(fod) anion was prepared in $d$-chloroform. $^1$H NMR spectra were obtained at 20, 30, and 40 °C as shown in Figure 58-60. Temperature change can be used to resolve overlapping signals of ortho hydrogen and diastereotopic methylene resonances. As the temperature increases from 20 °C to 40 °C, the overlapping resonances around 11-12 ppm showed resolution (Figure 60). The meta/para protons do not show any resolution with the variation of temperature. The results are summarized in Table XII.

Table XII. $^1$H NMR chemical shift of methyloctyiphenylsulfonium ion in the presence of Eu(tfc)$_3$(fod) as function of temperature.

<table>
<thead>
<tr>
<th></th>
<th>Ortho Protons</th>
<th>Meta/Para Protons</th>
<th>S-methyl Protons</th>
<th>Diastereotopic methylene protons</th>
</tr>
</thead>
<tbody>
<tr>
<td>20 °C</td>
<td>11.8 ppm</td>
<td>9.5 ppm</td>
<td>17.4 ppm</td>
<td>11.5 ppm</td>
</tr>
<tr>
<td>30 °C</td>
<td>11.2 ppm</td>
<td>9.2 ppm</td>
<td>16.3 ppm</td>
<td>10.8 ppm</td>
</tr>
<tr>
<td>40 °C</td>
<td>11 ppm</td>
<td>9 ppm</td>
<td>15.5 ppm</td>
<td>10.2 ppm</td>
</tr>
</tbody>
</table>
Figure 58. The $^1$H NMR spectrum of methyloctylphenylsulfonium tetrakis-(tfc)$_3$(fod)$^-$ europium (III) in CDCl$_3$ at 20 °C.
Figure 59. The $^1$H NMR spectrum of methyloctylphenylsulfonium tetrakis-(tfc)$_3$ (fod)$^-$ europium (III) in CDCl$_3$ at 30 °C.
Figure 60. The $^1$H NMR spectrum of methyloctylphenylsulfonium tetrakis-(tfc)$_3$(fod)$^-$ europium (III) in CDCl$_3$ at 40 °C.
E. Benzylmethylphenyl Sulfonium ion.

1. Benzylmethylphenylsulfonium tetrafluoroborate: The $^1$H NMR spectrum of this sulfonium salt in $d_6$-acetone is shown in Figure 61. The methyl peaks which are directly bonded to sulfur (S-methyl) are observed at 3.5 ppm. Due to the anisotropy of two aromatic ring, diastereotopic methylene protons go down field at about 5.1 ppm. The aromatic proton resonances of the benzyl group appear at about 7.3 ppm. The phenyl aromatic signals are exhibited about 7.8 ppm.

2. Tetrakis praseodymium anion-benzylmethylyphenylsulfonium cation pair: We investigated two kinds of praseodymium anions for this sulfonium salt: Pr(tfc)$_4^-$ and Pr(tfc)$_3$(fod)$^-$.

Ion Pair Formation with Pr(tfc)$_4^-$: A 0.1 M solution of the benzylmethylphenyl sulfonium cation-Pr(tfc)$_4$ anion was prepared in $d$-chloroform. $^1$H NMR spectra were obtained at 20 and 30 °C, as shown in Figures 62-63. Ortho hydrogen resonances exhibit no enantiomeric resolution. Diastereotopic methylene protons exhibit some resolution but, overall, good resolution cannot be obtained.

Ion Pair Formation with Pr(tfc)$_3$(fod)$^-$: A 0.1 M solution of the benzylmethylphenyl sulfonium cation-Pr(tfc)$_3$(fod)$^-$ anion was prepared in $d$-chloroform. $^1$H NMR spectra were obtained at 20 and 30 °C, as shown in Figures 64-65. Ortho hydrogen resonances exhibit no enantiomeric resolution. Diastereotopic methylene protons and S-methyl resonances can be seen with some resolution. Overall, good enantiomeric resolution cannot be obtained.
Figure 61. The $^1$H NMR spectrum of benzylmethylphenylsulfonium tetrafluoroborate in $d_6$-acetone.
Figure 62. The $^1$H NMR spectrum of benzylmethylphenylsulphonium tetrakis-(tfc)$_4^-$ praseodymium (III) in CDCl$_3$ at 20 °C.
Figure 63. The $^1$H NMR spectrum of benzylmethylphenylsulfonium tetrakis-(tfc)$_4^-$ praseodymium (III) in CDCl$_3$ at 30 °C.
Figure 64. The $^1$H NMR spectrum of benzylmethyphenylsulfonium tetrakis-(tfc)$_3$ (fod)$^-$ praseodymium (III) in CDCl$_3$ at 20 °C.
Figure 65. The $^1$H NMR spectrum of benzylmethylphenylsulfonium tetrakis-(tfc)$_3$(fod)$^-$ praseodymium (III) in CDCl$_3$ at 30 °C.
IV. CONCLUSIONS.

Among the shift reagents, Pr(tfc)$_4^+$ gave best enantiomeric resolutions for ethylmethyl phenyl- and methyloctylophenylsulfonium ions. In order to compare the effectiveness of the various shift reagents at providing enantiomeric resolution, we have compared the peak nonequivalence of the phenyl ortho hydrogen resonance (in ppm) for the various alkylmethyl phenylsulfonium ions. The results are summarized in Table XIII. It is abundantly clear that both Eu(tfc)$_4^+$ and Pr(tfc)$_4^+$ provide the best enantiomeric resolution overall for these racemic mixtures. The ligand hfc is clearly ineffective whether combined with Eu(III) or Pr(III) ion. The reason for this ligand effect is not clear.

Table XIII. Shift nonequivalence (ppm) for Ortho Hydrogen Resonances of Alkylmethylphenylsulfonium Ions.

<table>
<thead>
<tr>
<th>R</th>
<th>Pr(tfc)$_4^+$</th>
<th>Pr(tfc)$_3$(fod)$^*$</th>
<th>Pr(hfc)$_4^+$</th>
<th>Eu(tfc)$_4^+$</th>
<th>Eu(tfc)$_3$(fod)$^*$</th>
<th>Eu(hfc)$_4^+$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ethyl</td>
<td>0.43</td>
<td>0.15</td>
<td>0</td>
<td>0.27$^2$</td>
<td>0.63$^2$</td>
<td>0</td>
</tr>
<tr>
<td>Butyl</td>
<td>0.50</td>
<td>0.31</td>
<td>__________</td>
<td>__________</td>
<td>0.36</td>
<td>__________</td>
</tr>
<tr>
<td>Octyl</td>
<td>0.43</td>
<td>0.11</td>
<td>0</td>
<td>0.64</td>
<td>0.20</td>
<td>0</td>
</tr>
<tr>
<td>Benzyl</td>
<td>__________</td>
<td>0</td>
<td>__________</td>
<td>0.16</td>
<td>0</td>
<td>__________</td>
</tr>
</tbody>
</table>

1. 0.1 M concentration of shift reagent and sulfonium ion in $d$-chloroform.
2. See reference 90.
All spectra were strongly temperature-dependent. Specifically, the spectrum of the sulfonium ion was much more temperature dependent than the spectrum of the ligand attached to the lanthanide ion. This strong temperature dependence of the sulfonium ion spectrum allowed us to make assignments for many of the resonances. It can be explained that temperature change can affect conformational relationship between shift reagent and sulfonium salt, and the degree of ion-pairing in solution.

Perhaps a better technique for tracking sulfonium ion resonance is by incremental addition of the chiral shift concentration. The effect of concentration is much more dramatic than temperature change (Figure 19-22, Figure 48-51).

Another tool for establishing assignments is integration of the peak. However, some caution should taken since we have observed that integration values for particularly strongly shifted resonances (i.e. S-CH$_3$) are less than predicted relative to the integration values of weakly shifted resonances.

We also noticed a distinct steric effect as the nature of the alkyl group in sulfonium ions changed from ethyl to butyl to octyl. These results are summarized in Table XIV, where the change in chemical shift, $\Delta\delta$, of the phenyl ortho hydrogen and S-methyl resonances are listed using Pr(tfc)$_4$ as a shift reagent. The butyl and octyl resonances are clearly shifted less by this reagent compared to the ethyl and benzyl resonances. We attribute this to a steric effect of the alkyl groups which diminishes the interaction between the sulfonium ion and the shift reagent.
Table XIV. Change in Chemical shift of selected sulfonium ion resonances with \( \text{Pr(tfc)}_4^+ \), 0.1 M, 20 °C.

\[ \Delta \delta, \text{ ppm} \]

<table>
<thead>
<tr>
<th>R</th>
<th>Ortho hydrogen resonances</th>
<th>S-methyl resonance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ethyl group</td>
<td>11.0</td>
<td>30.9</td>
</tr>
<tr>
<td>Butyl group</td>
<td>4.2</td>
<td>11.6</td>
</tr>
<tr>
<td>Octyl group</td>
<td>3.5</td>
<td>9.4</td>
</tr>
<tr>
<td>Benzyl group</td>
<td>11.2</td>
<td>27.4</td>
</tr>
</tbody>
</table>

The ion-pairing technique developed in this research appears to be a reliable, rapid technique. In many instances, the resolved enantiomeric resonances were not base-lined resolved. Therefore it would be advisable to use line-fitting routines to determine relative areas so that enantiomeric excess can be determined.
BIBLIOGRAPHY.


