Diastereomeric Interaction of Partially Resolved Amines Facilitated by Lanthanide Chelates. Evidence for Dynamic Equilibrium between Seven-Coordinate and Eight-Coordinate Alkylamine–Lanthanide Chelate Adducts[1]

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Abstract: Enantiomeric shift differences were induced by achiral shift reagents in ^1H NMR for the partially resolved alkylamines. The origin of the shift differences was ascribed to the 1:2 adducts of lanthanide shift reagents and amines. The enantiomeric shift differences for various lanthanide reagent concentrations suggested the stoichiometric changes in solution. The equilibria between the 1:1 (seven-coordinate) and the 1:2 (eight-coordinate) adducts were established for the alkylamine complexes with europium, praseodymium, and ytterbium reagents.

Since the discovery of the lanthanide shift reagents by Hinckley,[2a] a vast number of studies of the application of lanthanide chelates in NMR spectroscopy have been conducted. At present, the application of lanthanide complexes as chemical shift inducers is a routine technique for ^1H NMR.[2b-4] The interpretation of the shifts induced by such reagents, however, requires knowledge about the factors influencing the induced shifts. These include the contributions due to contact shifts,[5-8] pseudocontact shifts,[9] complex formation shifts,[10-12] and the stoichiometry of the adduct. On the stoichiometry in solution, recent studies[13-18] suggested the existence of an equilibrium between a 1:1 and a 1:2 adduct of shift reagent and substrate. In the first investigation,[13] two rapid equilibria were assumed:

$$\mathrm{Ln} + \mathrm{S} \rightleftharpoons \mathrm{Ln{-}S}\ (K_1,\ \Delta_1)$$
$$\mathrm{Ln{-}S} + \mathrm{S} \rightleftharpoons \mathrm{Ln{-}S_2}\ (K_2,\ \Delta_2)$$

where Ln and S represent the shift reagent and substrate, respectively. Four parameters, two association equilibrium constants (K_1, K_2), and two limiting incremental shifts due to the shift reagent (Δ_1, Δ_2 in parts per million), were calculated to give an adequate account of the observed shift induced by the reagent at various concentrations. They showed rather definitively that assumption of just 1:1 complex formation gives very poor agreement between calculated and observed shifts. The procedures employed by the other authors are essentially similar.[15-18] Recently, Goering et al.[19] also suggested the presence of the equilibria of the 1:1 and 1:2 adducts from similar experiments using chiral shift reagents. These reports, however, present rather indirect evidence for such an equilibrium. It is the purpose of this report to provide more direct evidence for the equilibrium between the 1:1 and 1:2 shift reagent adducts of alkylamines.

Results and Discussion

As part of a general study of lanthanide shift reagents,[2b] their effects on partially resolved enantiomeric amines were investigated. In the course of this study, the methyl proton resonance of partially resolved α-phenylethylamine (**1**) was found to exhibit two sets of shifted doublets in the presence of Eu(fod)$_3$[20] (Figure 1a). Since it is generally accepted that the NMR spectra of a racemate and of either enantiomer in pure form are identical in achiral media, this observation warranted further investigation.

When substituting Eu(dpm)$_3$[20] and Yb(fod)$_3$ as the shift reagents, similar results were obtained, although, in the latter case, severe line broadening caused collapse of the doublet structure (Figures 1b and 1c). Upon measuring the ratio of the signal areas for the two sets of resonances, it was found that this ratio was equal to the ratio of the two enantiomers in the partially resolved mixture. This led us to believe that the two sets of resonances were due to each of the enantiomers. The same results were also found for other optically active amines such as α-(2-thienyl)ethylamine (**2**) (Figure 2). Apparently these observations are quite similar to those very recently reported by Whitesides et al.[21] They found that racemic *N*-methyl-α-phenylethylamine exhibited an enantiomeric shift difference induced by Eu(fod)$_3$ when optically pure α-phenylethylamine was present. Our finding therefore indicates that addition of an optically active amine other than the solute is not a prequisite for inducing enantiomeric shift differences.

The enantiomeric shift differences ($\Delta\Delta\delta$), as well as the ratio of the areas, was studied as a function of the relative concentration of the two enantiomers. The $\Delta\Delta\delta$ values were found to depend not only on the ratio of the enantiomers but also on the relative concentration of amine (substrate) and shift reagent. The $\Delta\Delta\delta$ values for the methyl proton resonances of **1** are listed in Table I for different ratios of the enantiomers. The variation of the same $\Delta\Delta\delta$ value with the relative concentration of amine and shift reagent is shown in Figure 3. Although the values differ for the two shift reagents listed, it is clear that the same dependence is observed, and that a maximum $\Delta\Delta\delta$ value is found at a molar ratio of shift reagent to substrate of ~0.5.

A previous report by Williams et al.[22] suggested an explanation for these observations. They found the NMR spectra of optically pure and of racemic dihydroquinine to be significantly different at the same concentration in deuteriochloroform. In addition, partially resolved dihydroquinine gave two sets of peaks for some proton resonances, the ratio of these peak areas being equal to the ratio of the enantiomer concentrations. These findings were rationalized by consideration of unusually strong solute–solute interaction for this compound.

A similar explanation would be applicable for the present observations. α-Phenylethylamine by itself cannot experience a sufficiently strong solute–solute interaction at the concentration we studied, as is apparent from the finding that either of pure enantiomers shows exactly the same proton NMR spectrum as the racemate. The dissymmetric interactions could, however, be facilitated by a lanthanide

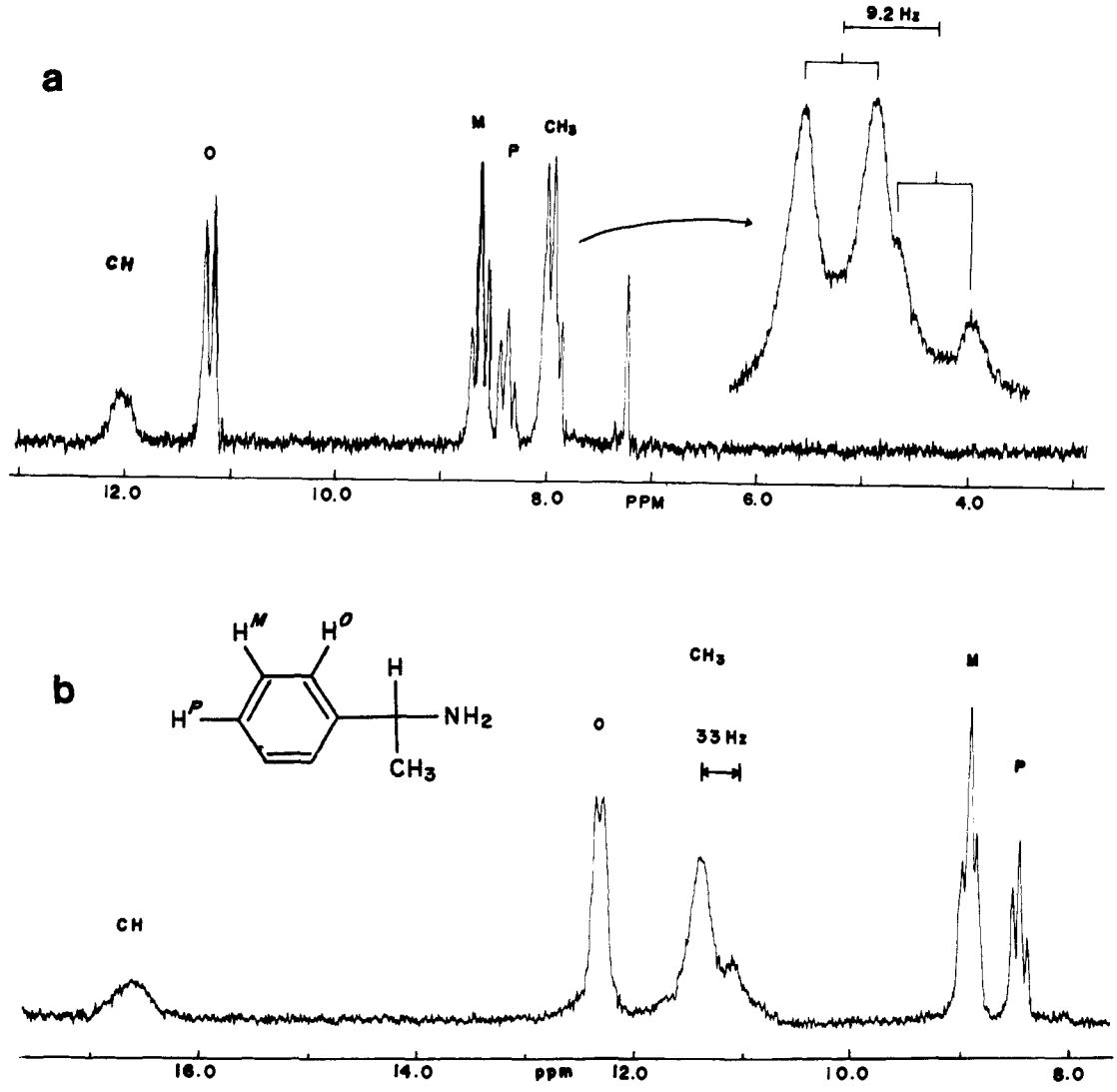
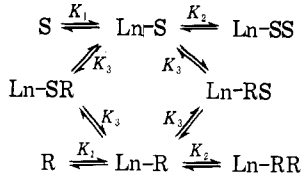


Figure 1. Room-temperature, 100-MHz NMR spectra of partially resolved α-phenylethylamine in $CDCl_3$ (the total amine concentrations was 0.1 *M* and the enantiomeric ratio was S/R = 0.2): (a) in the presence of 0.05 *M* $Eu(fod)_3$; (b) in the presence of 0.01 *M* $Yb(fod)_3$.

complex as an intermediate. The origin of the enantiomeric shift differences may be explained by invoking a series of equilibria:



where Ln represents the lanthanide shift reagent and S and R are the two enantiomers. K_1 represents the equilibrium of the 1:1 complexes, and K_2 and K_3 represent the equilibria of the 1:2 complexes. Ln-RR and Ln-SS constitute the *dl* pair, and Ln-SR and Ln-RS the meso form of the diastereomeric set of complexes. If rapid equilibria are assumed, the chemical-shift difference, $\Delta\Delta\delta$, can be expressed by eq 1. The details in the derivation of this and subsequent equations can be found in Appendix I. It follows immediately that (1) in a racemic mixture, where [S] = [R], there is not observable chemical-shift difference, (2) even if the induced chemical shifts of the diastereomeric forms are identical, it is possible to observe a chemical-shift difference, provided $K_2 \neq K_3$, and (3) even if $K_2 = K_3$, there will be a chemical-shift difference provided there is a difference in induced chemical shift between the meso form and the *dl* pair. Although the first point is somewhat obvious, it is important to note that the induced shifts in the racemate may differ from those in the optically pure solutions since the δ_{Ln-RR} and δ_{Ln-SR} may differ.

$$\Delta\Delta\delta = \frac{[Ln][S][R]([S] - [R])K_1K_3}{C_RC_S}\{2(K_2/K_3 - 1) \times (\delta_R + [Ln]K_1\delta_{Ln-R}) + 2[Ln]K_1K_2([S] + [R]) \times (2\delta_{Ln-SR} - 2\delta_{Ln-RR}) + (1 + [Ln]K_1) \times (2\delta_{Ln-SR} - 2(K_2/K_3)\delta_{Ln-RR})\} \quad (1)$$

For partially resolved amines, a chemical-shift difference was observed, and it remains to ascertain the origin of this. Modification of eq 1 in the limits of $\delta_{Ln-RR} \neq \delta_{Ln-SR}$, but $K_2 = K_3$ and $\delta_{Ln-RR} = \delta_{Ln-SR}$, but $K_2 \neq K_3$ gives eq 2 and 3

(i) $\delta_{Ln-RR} = \delta_{Ln-SR}$; $K_2 \neq K_3$

$$\Delta\Delta\delta = 2\frac{[Ln][S][R]K_1K_3([S] - [R])}{C_RC_S}(K_2/K_3 - 1) \times \{(\delta_R - \delta_{Ln-RR}) + K_1[Ln](\delta_{Ln-R} - \delta_{Ln-RR})\} \quad (2)$$

(ii) $\delta_{Ln-RR} \neq \delta_{Ln-SR}$; $K_2 = K_3$

$$\Delta\Delta\delta = 2\frac{C_S - C_R}{C_SC_R}[Ln\text{-}SR](\delta_{Ln-SR} - \delta_{Ln-RR}) = \frac{1 - 2X_R}{X_R}2\frac{[Ln\text{-}RR]}{C_R}(\delta_{Ln-SR} - \delta_{Ln-RR}) \quad (3)$$

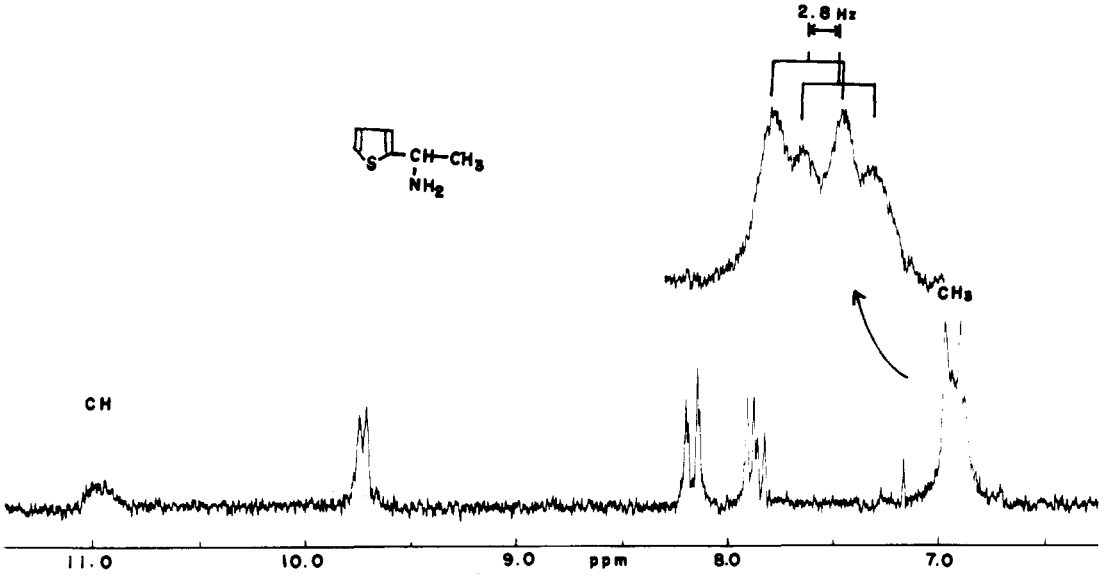


Figure 2. Room-temperature, 100-MHz NMR spectra of partially resolved α-(2-thienyl)ethylamine in $CDCl_3$ in the presence of 0.03 *M* $Eu(fod)_3$ (the total amine concentration was 0.1 *M*, and the enantiomeric ratio was S/R = 0.5).

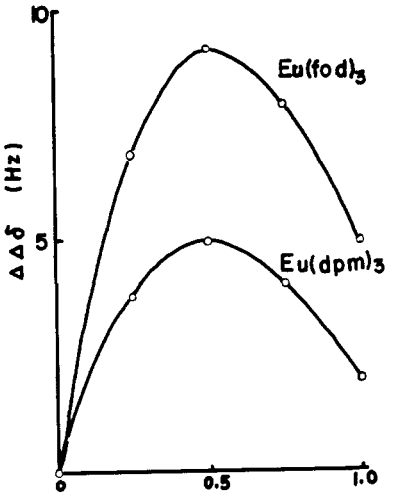


Figure 3. The enantiomeric shift difference for the methyl protons of **1** as a function of the molar ratio of shift reagent to total amine (the total amine concentration was kept at 0.1 *M*, and the enantiomeric ratio was constant at 0.2).

Table 1. Enantiomeric Shift Differences, $\Delta\Delta\delta$, of α-Phenylethylamine at a Constant Ratio of $Eu(fod)_3$ to Total Amine

C_{Ln}, *M*	$C_S + C_R$, *M*	C_S/C_R	$\Delta\Delta\delta$, Hz
0.05	0.1	0.6	2.9
0.05	0.1	0.5	4.2
0.05	0.1	0.4	6.4
0.05	0.1	0.2	9.2
0.05	0.1	0.1	10.5

3. Considering eq 2, it follows that the largest chemical-shift difference should be observed for the protons with the largest induced shift. In this case, this is the α-methine proton. Although this signal is somewhat broadened, it is clear from Figure 1 that the linewidth is less than what would be expected based on the chemical-shift difference for the methyl protons. The conclusion must then be that the overriding factor in causing the chemical-shift difference is the

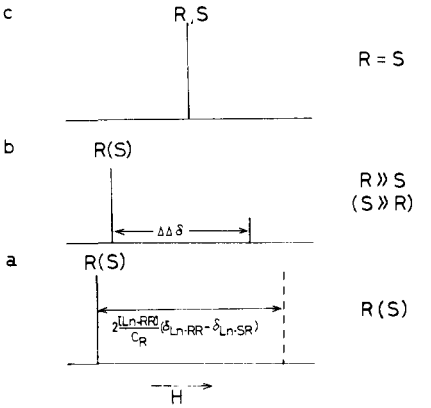


Figure 4. Diagrammatic representation of the induced shifts for the methyl protons of **1**.

difference in induced shift of the Ln–RR and Ln–SR forms. An assumption that $K_2 = K_3$ should thus be a good one, and from eq 3, it is seen that the values of $\delta_{Ln\text{-}SR}$ and $\delta_{Ln\text{-}RR}$ are important factors determining the chemical-shift difference. Equation 3 also shows the dependence on the extent of resolution of the enantiomers, i.e., the ratio of R to S forms. This dependence agrees well with the observed changes listed in Table I. Considering the second part of eq 3 we can see that as X_R becomes close to unity, $[Ln\text{-}RR]/C_R$ maximizes, and $(1 - 2X_R)/X_R$ approaches −1. Hence, if C_{Ln}/C is kept constant at 0.5, $[Ln\text{-}RR]/C_R$ will approach 0.5 as a maximum value. With this condition it is possible to estimate a "minimum" value for $(\delta_{Ln\text{-}SR} - \delta_{Ln\text{-}RR})$ since $(\Delta\Delta\delta)_{X_R \to 1} \to (\delta_{Ln\text{-}RR} - \delta_{Ln\text{-}SR})$. In this manner, the "minimum" value is found to be $(\delta_{Ln\text{-}SR} - \delta_{Ln\text{-}RR}) = (-)11$ Hz for the α-methyl protons of **1** with $Eu(fod)_3$.[23] In addition, if desired, it is then possible from the first part of eq 3 to estimate [Ln-SR] as a function of the molar ratio. Thus it is possible to obtain a "real" value for $(\delta_{Ln\text{-}SR} - \delta_{Ln\text{-}RR})$. The origin of the enantiomeric shift difference, and its relation to the formula given, can be understood using a diagramatic representation of the averaged shift given by eq I and II (Appendix I). Figure 4a shows the expected signal from either of the pure enantiomers. The upfield position, indicated by a broken line, represents the expected chemical shift of the Ln-SR species ($\delta_{Ln\text{-}SR}$).

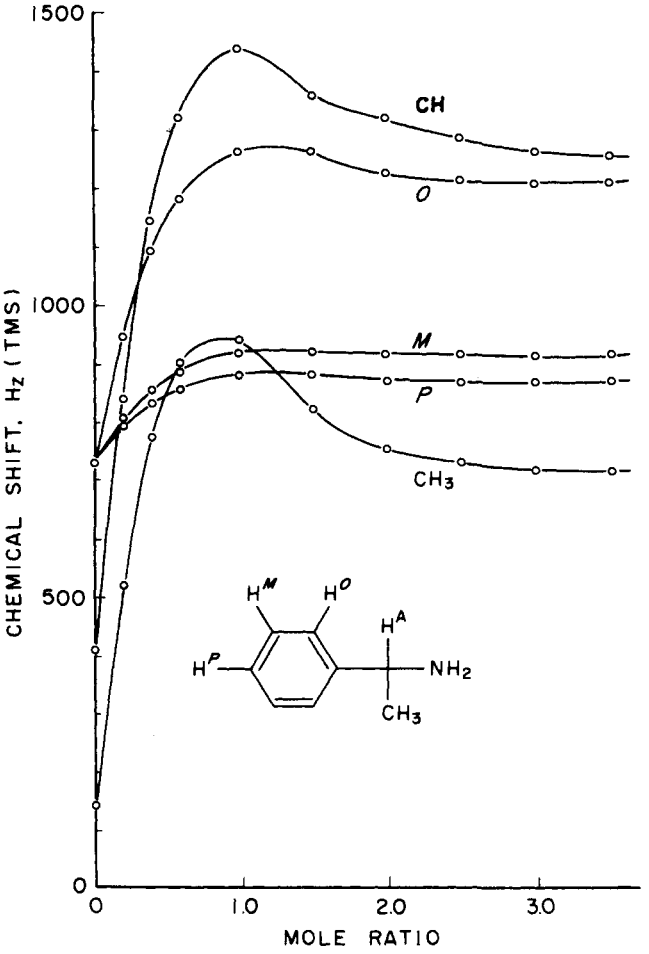


Figure 5. Chemical shifts at 100 MHz for 0.1 *M* pure L-α-phenylethylamine (S) as a function of the molar ratio of shift reagent [Eu(fod)$_3$] to amine.

Upon addition of a small amount of the other enantiomer, the contributions from each will average differently with the Ln-SR species, and the induced shift for the minor component will appear upfield (Figure 4b). In the limit of a racemic mixture, the two enantiomers will average equally, and there will be only one signal at the center position (Figure 4c). A direct consequence of this is that the induced chemical shifts for the racemic mixture are not the same as those for the pure enantiomers. However, the measurements of the induced chemical shifts have errors which are as large or larger than the expected difference between the racemic and pure enantiomer (ca. 5 Hz), so the difference cannot be established with certainty.

The assumption that $K_2 = K_3$ implies that the binding of the S and R enantiomers is equally favorable energetically, and therefore the stability of each of the diastereomeric complexes is identical. In actual fact, this does not have to be the case, and a small difference between K_2 and K_3 could give a contribution, which in some cases conceivably could be of major importance.

The formation of 1:2 complexes, as this explanation suggests, requires the existence of an eight-coordinate lanthanide complex. In the crystalline state, evidence for such eight-coordinated complexes has been found by X-ray crystallographic technique.[24-26] In solutions, however, most of the evidence for eight-coordinate complexes is rather indirect.[13-19] The clearest evidence seems to be provided by Evans and Wyatt.[27] They observed separate methyl signals from free and complexed dimethyl sulfoxide (DMSO) in the presence of Eu(fod)$_3$ at −80°, and from the signal intensities concluded that, with excess DMSO, a 1:2 complex of shift reagent to DMSO (an eight-coordinate complex) predominated. At room temperature with excess Eu(dpm)$_3$, a 1:1 complex (a seven-coordinate complex) is obtained. Similarly Uebel and Wing[28] isolated a seven-coordinate lanthanide complex with sulfoxide, which had been characterized by X-ray analysis. These observations render some support to our suggestion that a rapid equilibrium between a seven- and eight-coordinate complex is present with these amines.

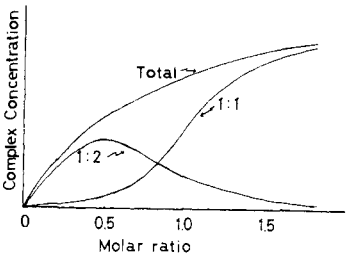


Figure 6. Schematic representation of the concentration of the 1:1 and 1:2 complexes in a solution as a function of the molar ratio of shift reagent to substrate.

The suggested explanation also requires that K_2 (and K_3) be sufficiently large that the concentration of 1:2 complexes will be significant. Whether this requirement is fulfilled depends on the relative stability of the seven- and eight-coordinate complexes. That there is only moderate or small differences in this relative stability seems evident from studies of other seven- and eight-coordinate complexes.[14] There is then no reason to expect that K_2 will be very small compared with K_1 in these amine complexes, and further evidence for this is found in the variation of the induced shifts with the molar ratio of lanthanide shift reagent to substrate. This variation is illustrated in Figure 5 for **1** and is found to be qualitatively very similar to previously observed changes.[13,14,29] The variation of this type has been analyzed in detail for several cases,[13,14] and in each, the conclusion was reached that 1:2 complexes were formed to a significant extent.

In addition, the formation of 1:2 complexes will naturally depend on the ratio of K_1 to K_2 as noted, but it is reasonable to expect a variation of each as illustrated qualitatively in Figure 6, where the maximum concentration of 1:2 complexes would occur at a molar ratio of shift reagent to substrate of 0.5. In qualitative terms, it is then easy to understand the variation of $\Delta\Delta\delta$ (Figure 3) as observed for **1** since the $\Delta\Delta\delta$ is directly proportional to the mole fraction of Ln-SR, which is maximum at $[C_{Ln}]/[C] = 0.5$.

There is therefore much evidence supporting the conclusion that, in solution of aliphatic amines and lanthanide shift reagents, a set of rapid equilibria between 1:1 and 1:2 adducts exists, and if partially resolved enantiomeric amines are used, these equilibria will fully account for observations of enantiomeric chemical-shift differences.

Experimental Section

100-MHz NMR spectra were measured on a Varian XL-100 spectrometer at ambient probe temperature using Me_4Si as an internal standard. All samples were dissolved in deuteriochloroform which had been dried over molecular sieves. Optically active and racemic α-phenylethylamine were purchased from Aldrich Chemicals (Gold Label grade) and were distilled prior to use. Partially resolved α-(2-thienyl)ethylamine was kindly provided by Dr W. H. Pirkle and was used without further purification. Shift reagents were purchased from Bio-Rad Laboratories and were used without any other drying procedure.

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Appendix I

For the set of equilibria proposed, the equilibrium constants are given by:

$$K_1 = \frac{[\text{Ln–S}]}{[\text{Ln}][\text{S}]} = \frac{[\text{Ln–R}]}{[\text{Ln}][\text{R}]}$$

$$K_2 = \frac{[\text{Ln–SS}]}{[\text{Ln–S}][\text{S}]} = \frac{[\text{Ln–RR}]}{[\text{Ln–R}][\text{R}]}$$

$$K_3 = \frac{[\text{Ln–SR}]}{[\text{Ln–S}][\text{R}]} = \frac{[\text{Ln–RS}]}{[\text{Ln–R}][\text{S}]}$$

In addition, it is clear that the total concentrations are:

$$C_{\text{Ln}} = [\text{Ln}] + [\text{Ln–S}] + [\text{Ln–R}] + [\text{Ln–RR}] + [\text{Ln–SS}] + [\text{Ln–SR}] + [\text{Ln–RS}]$$

$$C_{\text{R}} = [\text{R}] + [\text{Ln–R}] + [\text{Ln–SR}] + [\text{Ln–RS}] + 2[\text{Ln–RR}]$$

$$C_{\text{S}} = [\text{S}] + [\text{Ln–S}] + [\text{Ln–SR}] + [\text{Ln–RS}] + 2[\text{Ln–SS}]$$

$$C = C_{\text{R}} + C_{\text{S}}$$

Assuming all the equilibria are rapid, the observed induced chemical shifts for each of the enantiomers will be given by[13] eq I and II. Experimentally it has been observed that

$$\Delta\delta_{\text{R}}^{\text{obsd}} = \frac{1}{C_{\text{R}}}([\text{R}]\delta_{\text{R}} + [\text{Ln–R}]\delta_{\text{Ln–R}} + 2[\text{Ln–RR}]\delta_{\text{Ln–RR}} + [\text{Ln–RS}]\delta_{\text{Ln–RS}} + [\text{Ln–SR}]\delta_{\text{Ln–SR}}) \quad \text{(I)}$$

$$\Delta\delta_{\text{S}}^{\text{obsd}} = \frac{1}{C_{\text{S}}}([\text{S}]\delta_{\text{S}} + [\text{Ln–S}]\delta_{\text{Ln–S}} + 2[\text{Ln–SS}]\delta_{\text{Ln–SS}} + [\text{Ln–RS}]\delta_{\text{Ln–RS}} + [\text{Ln–SR}]\delta_{\text{Ln–SR}}) \quad \text{(II)}$$

the chemical shifts of each of the pure enantiomers are identical, which implies that $\delta_{\text{R}} = \delta_{\text{S}}$. In an excess of lanthanide shift reagent, it is also observed that the induced chemical shifts of each of the pure enantiomers are identical, which must mean that $\delta_{\text{Ln–RR}} = \delta_{\text{Ln–SS}}$. All of these equalities are chemically intuitive since the complexes are enantiomeric to each other. It does not, however, necessarily follows that $\delta_{\text{Ln–RR}} = \delta_{\text{Ln–SR}}$, whereas it is assumed that $\delta_{\text{Ln–SR}} = \delta_{\text{Ln–RS}}$ since Ln-SR and Ln-RS are identical, but Ln-RR (or Ln-SS) and Ln-SR are diastereomeric. Using these considerations, the enantiomeric shift difference, $\Delta\Delta\delta$, is given by eq III. Equation III can be rearranged to give eq IV. As discussed in the text, two limits can be considered.

$$\Delta\Delta\delta = \delta_{\text{R}}^{\text{obsd}} - \delta_{\text{S}}^{\text{obsd}} = ([\text{R}]/C_{\text{R}} - [\text{S}]/C_{\text{S}})(\delta_{\text{R}} + K_1[\text{Ln}]\delta_{\text{Ln–R}}) + 2[\text{Ln}]K_1K_2([\text{R}]^2/C_{\text{R}} - [\text{S}]^2/C_{\text{S}})\delta_{\text{Ln–RR}} + 2[\text{Ln}]K_1K_3([\text{R}][\text{S}]/C_{\text{R}} - [\text{R}][\text{S}]/C_{\text{S}})\delta_{\text{Ln–SR}} \quad \text{(III)}$$

$$\Delta\Delta\delta = \frac{1}{C_{\text{R}}C_{\text{S}}}\{[\text{Ln}]K_1(2K_2 - 2K_3)[\text{S}][\text{R}]([\text{S}] - [\text{R}]) \times (\delta_{\text{R}} + K_1[\text{Ln}]\delta_{\text{Ln–R}}) - [\text{Ln}]K_1K_2[\text{S}][\text{R}]([\text{S}] - [\text{R}]) \times (1 + [\text{Ln}]K_1 + 2[\text{Ln}]K_1K_3([\text{S}] + [\text{R}])2\delta_{\text{Ln–RR}}) + [\text{Ln}]K_1K_3[\text{S}][\text{R}]([\text{S}] - [\text{R}])(1 + [\text{Ln}]K_1 + 2[\text{Ln}]K_1K_2([\text{S}] + [\text{R}])2\delta_{\text{Ln–SR}})\}$$

$$= \frac{[\text{Ln}][\text{S}][\text{R}]([\text{S}] - [\text{R}])K_1K_3}{C_{\text{R}}C_{\text{S}}}\{2(K_2K_3 - 1)(\delta_{\text{R}} + [\text{Ln}]K_1\delta_{\text{Ln–R}}) + 2[\text{Ln}]K_1K_2([\text{S}] + [\text{R}])(2\delta_{\text{Ln–SR}} - 2\delta_{\text{Ln–RR}}) + (1 + [\text{Ln}]K_1)(2\delta_{\text{Ln–SR}} - 2(K_2/K_3)\delta_{\text{Ln–RR}})\} \quad \text{(IV)}$$

(i) $\delta_{\text{Ln–SR}} = \delta_{\text{Ln–RR}}$, but $K_2 \neq K_3$; with these conditions, we get eq V. From this expression, it is clear that there should be an enantiomeric shift difference for all protons in the compound.

$$\Delta\Delta\delta = \frac{[\text{Ln}][\text{S}][\text{R}]([\text{S}] - [\text{R}])K_1K_3}{C_{\text{R}}C_{\text{S}}}\{2(K_2/K_3 - 1)(\delta_{\text{R}} + K_1[\text{Ln}]\delta_{\text{Ln–R}}) + (1 + [\text{Ln}]K_1)(1 - K_2/K_3)2\delta_{\text{Ln–RR}}\}$$

$$= \frac{[\text{Ln}][\text{S}][\text{R}]([\text{S}] - [\text{R}])K_1K_3}{C_{\text{R}}C_{\text{S}}}(K_2/K_3 - 1) \times \{(2\delta_{\text{R}} - 2\delta_{\text{Ln–RR}}) + K_1[\text{Ln}](2\delta_{\text{Ln–R}} - 2\delta_{\text{Ln–RR}})\} \quad \text{(V)}$$

(ii) $\delta_{\text{Ln–SR}} \neq \delta_{\text{Ln–RR}}$, but $K_2 = K_3$; with these conditions, we get eq VI, where X_{R} denotes the mole fraction of the R enantiomer in the partially resolved amine.

$$\Delta\Delta\delta = \frac{[\text{Ln}][\text{S}][\text{R}]([\text{S}] - [\text{R}])K_1K_3}{C_{\text{R}}C_{\text{S}}}\{2[\text{Ln}]K_1K_2 \times ([\text{S}] + [\text{R}]) + 1 + [\text{Ln}]K_1\}(2\delta_{\text{Ln–SR}} - 2\delta_{\text{Ln–RR}})$$

$$= \{[\text{Ln–SR}]/C_{\text{R}}C_{\text{S}}\}\{2[\text{Ln}][\text{S}]^2K_1K_2 + [\text{Ln}][\text{S}]K_1 + [\text{S}] + 2[\text{Ln–SR}] - 2[\text{Ln}][\text{R}]^2K_1K_2 - [\text{Ln}][\text{R}]K_1 - [\text{R}] - 2[\text{Ln–SR}]\}2(\delta_{\text{Ln–SR}} - \delta_{\text{Ln–RR}})$$

$$= \{2(C_{\text{S}} - C_{\text{R}})/C_{\text{S}}C_{\text{R}}\}[\text{Ln–SR}](\delta_{\text{Ln–SR}} - \delta_{\text{Ln–RR}})$$

$$= \{(1 - 2X_{\text{R}})/X_{\text{R}}\}2\{[\text{Ln–RR}]/X_{\text{R}}\}(\delta_{\text{Ln–SR}} - \delta_{\text{Ln–RR}})$$

References and Notes

(1) A major portion of this study was presented at the NMR Symposium of Japan, held at Osaka, Oct 10, 1972.
(2) (a) C. C. Hinckley, *J. Am. Chem. Soc.*, **91**, 5160 (1969); (b) M. Kainosho and K. Ajisaka, *J. Synth. Org. Chem. Jpn.*, **31**, 126 (1973).
(3) R. Ammon and D. Fischer, *Angew. Chem., Int. Ed. Engl.*, **11**, 675 (1972).
(4) A. F. Cockerill, G. L. O. Davies, R. C. Harden, and D. M. Backham, *Chem. Rev.*, **73**, 553 (1973).
(5) K. Ajisaka and M. Kainosho, *J. Am. Chem. Soc.*, **97**, 330 (1975).
(6) K. Tori, Y. Yoshimura, M. Kainosho, and K. Ajisaka, *Tetrahedron Lett.*, 1573 (1973).
(7) O. A. Gansow, P. A. Loeffler, R. E. Davies, M. R. Willcott, III, and R. E. Lenkinski, *J. Am. Chem. Soc.*, **95**, 3389, 3390 (1973).
(8) G. H. Hawkes, C. Marzin, S. R. Johns, and J. D. Roberts, *J. Am. Chem. Soc.*, **95**, 1661 (1973).
(9) H. M. McConnell and R. E. Robertson, *J. Chem. Phys.*, **29**, 1361 (1958).
(10) B. Bleaney, C. M. Dobson, B. A. Levine, R. B. Martin, R. J. P. Williams, and A. Xavier, *J. Chem. Soc., Chem. Commun.*, 791 (1972).
(11) K. Ajisaka, M. Kainosho, H. Sigemoto, K. Tori, Z. W. Wolkowski, and Y. Yoshimura, *Chem. Lett.*, 1205 (1973).
(12) K. Tori, Y. Yoshimura, M. Kainosho, and K. Ajisaka, *Tetrahedron Lett*, 3127 (1973).
(13) B. L. Shapiro and M. D. Johnston, Jr., *J. Am. Chem. Soc.*, **94**, 8185 (1972).
(14) K. Roth, M. Grosse, and D. Rewicki, *Tetrahedron Lett.*, 435 (1972).
(15) B. L. Shapiro, M. D. Johnston, Jr., and M. J. Shapiro, *Org. Magn. Reson.*, **5**, 21 (1973).
(16) V. G. Gibb, I. M. Armitage, L. D. Hall, and A. G. Marshall, *J. Am. Chem. Soc.*, **94**, 8919 (1972).
(17) A. Arduini, I. M. Armitage, L. D. Hall, and A. G. Marshall, *Carbohydr. Res.*, **31**, 255 (1973).
(18) J. Reuben, *J. Am. Chem. Soc.*, **95**, 3534 (1973).
(19) H. L. Goering, J. N. Eikenberry, G. S. Koermer, and C. J. Lattimer, *J. Am. Chem. Soc.*, **96**, 1493 (1974).
(20) Eu(fod)$_3$ and Eu(dpm)$_3$ represent tris(1,1,1,2,2,3,3-heptafluoro-7,7-dimethyl-4,6-dionato)europium(III) and tris(dipivalomethanato)europium(III), respectively.
(21) M. D. McCreary, D. W. Lewis, D. L. Wernick, and G. M. Whitesides, *J. Am. Chem. Soc.*, **96**, 1038 (1974).
(22) T. Williams, R. G. Ritcher, P. Bommer, J. Gutzwiller, and M. Uskokovic, *J. Am. Chem. Soc.*, **91**, 1871 (1969).
(23) This value is expected to be both temperature and concentration dependent, and experimentally this was verified. In fact a fivefold dilution gave rise to approximately 20% reduction of $\Delta\Delta\delta$. Such a decrease could also in part be from the effect of competitive solvation by chloroform.[16]
(24) W. D. Horrocks, Jr., and J. P. Sipe, III, *J. Am. Chem. Soc.*, **93**, 6800 (1971).
(25) W. D. Horrocks, Jr., J. P. Sipe, III, and J. R. Labor, *J. Am. Chem. Soc.*, **93**, 5258 (1971).
(26) R. E. Cramer and K. Seff, *Acta Crystallogr., Sect. B*, **28**, 3821 (1972).
(27) D. E. Evans and M. Wyatt, *J. Chem. Soc., Chem. Commun.*, 312 (1972).
(28) J. J. Uebel and R. M. Wing, *J. Am. Chem. Soc.*, **94**, 8910 (1972).
(29) J. K. M. Sanders, S. W. Hanson, and D. H. Williams, *J. Am. Chem. Soc.*, **94**, 5325 (1972).