Table IV

Amino acids	k_{C_0}[a]	$k_{C\alpha}$[a]	k_{C_0}[a] + $k_{C\alpha}$[a]	K_{C_0}	$\Delta\delta C_0/(\Delta\delta C_0 + \Delta\delta C\alpha)$	$K_{C\alpha}$	$\Delta\delta C_0/(\Delta\delta C_0 + \Delta\delta C\alpha)$
Alanine	−0.57	−0.34	−0.91	0.626	0.632	0.373	0.367
Leucine	−0.51	−0.35	−0.86	0.593	0.590	0.407	0.409
Valine	−0.49	−0.39	−0.88	0.556	0.565	0.443	0.434
Isoleucine	−0.51	−0.40	−0.91	0.560	0.541	0.439	0.459

[a] k_i being expressed in ppm/Hz.

the sum $k_{C_0} + k_{C\alpha}$ is appreciably the same for all the amino acids studied; $k_{C_0} + k_{C\alpha} = 0.88 \pm 0.03$ ppm/Hz.

The constants k_{C_0} and $k_{C\alpha}$ can thus be standardized by posing

$$K_{C_0} + K_{C\alpha} = 1 \tag{7}$$

where the standardized values K_{C_0} and $K_{C\alpha}$ are given by the equations

$$K_{C_0} = \frac{k_{C_0}}{k_{C_0} + k_{C\alpha}} \tag{8}$$

and

$$K_{C\alpha} = \frac{k_{C\alpha}}{k_{C_0} + k_{C\alpha}} \tag{9}$$

From expressions 4, 8, and 9 we can write

$$K_{C_0} = \frac{k_{C_0}}{k_{C_0} + k_{C\alpha}} = \frac{\Delta\delta C_0}{\Delta\delta C_0 + \Delta\delta C_\alpha} \tag{10}$$

$$K_{C\alpha} = \frac{k_{C\alpha}}{k_{C_0} + k_{C\alpha}} = \frac{\Delta\delta C_\alpha}{\Delta\delta C_0 + \Delta\delta C_\alpha} \tag{11}$$

where $\Delta\delta C_i$ is the difference between the chemical shifts of the carbon C_i corresponding to the COOH and COO^- states. It is observed in eq 10 and 11 that the standardized values K_{C_0} and $K_{C\alpha}$ are independent of $J_{C_0-C\alpha}$. The K_{C_0} and $K_{C\alpha}$ values for each of the amino acids are listed in Table IV. In principle they should be equal to those determined from the ratio $\Delta\delta C_i/(\Delta\delta C_0 + \Delta\delta C_\alpha)$ (Table IV), the slight differences being ascribable to the error on the estimation of $\Delta\delta C_i$ measured on the titration curve between acid and neutral pH.

From $J_{C_0-C\alpha}$ it is, therefore, possible to deduce δC_0 and δC_α on the one hand and the proportions of COOH and COO^- in equilibrium in the solution on the other. For ^{13}C products in natural abundance where the ^{13}C signal of C_0 is difficult to observe, the value $\Delta\delta C_0$ can be obtained by using that of $\Delta\delta C_\alpha$; knowing δC_α it is hence possible to calculate δC_0.

Direct Determination of Enantiomeric Compositions with Optically Active Nuclear Magnetic Resonance Lanthanide Shift Reagents[1a,2]

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Abstract: Tris(3-trifluoroacetyl-*d*-camphorato)europium(III), Eu(facam)$_3$, tris(3-heptafluorobutyryl-*d*-camphorato)-europium(III), Eu(hfbc)$_3$, and the corresponding praseodymium analogs, Pr(facam)$_3$ and Pr(hfbc)$_3$, are useful nmr shift reagents for direct determination of enantiomeric compositions. These optically active shift reagents are applicable to those classes of compounds that respond to conventional shift reagents such as Eu(dpm)$_3$ and Eu(fod)$_3$. In the presence of the above optically active lanthanide chelates, enantiomers have nonequivalent nmr spectra, and shift differences for enantiotopic protons of over 1 ppm have been observed. Generally, shift differences are large enough for complete separation of at least one set of enantiotopic signals, and enantiomeric compositions (optical purities) can be determined directly from relative peak areas. The hfbc chelates induce larger shifts than the facam chelates. However, shift differences for enantiomers are not consistently larger for a particular reagent. Also, magnitudes of nonequivalence vary with the shift-reagent–substrate ratio in unpredictable ways.

The use of optically active nmr lanthanide shift reagents for direct determination of enantiomeric compositions has been the subject of several recent communications.[3-6] We now complete our initial report[4] and present additional pertinent results of our work in this area.

(1) (a) Supported in part by grants from the National Science Foundation (GP21116X) and the Air Force Office of Scientific Research (AFOSR-71-1972); (b) National Institutes of Health Predoctoral Fellow, 1968–1971.

(2) Presented in part at the 165th National Meeting of the American Chemical Society, Dallas, Texas, April 1973.

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(5) (a) R. R. Fraser, M. A. Petit, and J. K. Saunders, *Chem. Commun.*, 1450 (1971); (b) R. R. Fraser, M. A. Petit, and M. Miskow, *J. Amer. Chem. Soc.*, **94**, 3253 (1972).

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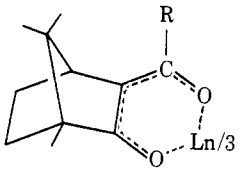
The optically active shift reagents that we have found most useful are four lanthanide chelates of the type illustrated by structure I. These are tris(3-trifluoro-

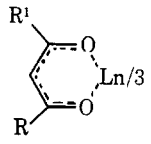


I

$Ln(facam)_3$, R = CF_3
$Ln(hfbc)_3$, R = C_3F_7

acetyl-*d*-camphorato)europium(III), $Eu(facam)_3$, tris-(3-heptafluorobutyryl-*d*-camphorato)europium(III), $Eu(hfbc)_3$, and the corresponding praseodymium analogs, $Pr(facam)_3$ and $Pr(hfbc)_3$.[2,4] The two β-diketone ligands are easily prepared and the europium and praseodymium chelates are very soluble in nonpolar solvents. In the presence of these optically active chelates, enantiomers (that respond to lanthanide nmr shift reagents) generally have nonequivalent nmr spectra. Usually, by proper choice of shift reagent and conditions, shift differences for at least one set of enantiotopic protons are large enough and separated from other signals so that enantiomeric compositions can be determined directly from relative peaks areas.

Other optically active europium chelates were also examined including those derived from 3-formyl-*d*-camphor (I, R = H), 3-carbethoxyacyl-*d*-camphor (I, R = carbethoxy), 2-formyl-(+)-pulegone, and 2-formyl-(+)-carvone. These β-diketone ligands[3,4] and chelates[7] were prepared by conventional methods. These chelates induced only small shifts in the nmr spectrum of 2-butanol and nonequivalence was not observed. Tris-(3,7-dimethyl-3,7-diphenyl-4,6-nonanedionato)-europium(III) (II, R = R′ = $C(CH_3)(C_2H_5)(C_6H_5)$), de-



II

rived from optically pure (*R*,*R*)-(−)-3,7-diphenyl-4,6-nonanedione, was also investigated. The optically pure β-diketone was prepared from (*R*)-(−)-2-methyl-2-phenylbutanoic acid.[8] The acid was converted to (*R*)-(−)-methyl 2-methyl-2-phenylbutanoate[8c] and (*R*)-(−)-3-methyl-3-phenyl-2-pentanone,[8a] which in turn were converted to the β-diketone by a standard method.[9] The europium chelate induced appreciable downfield shifts in the nmr spectra of 2-butanol and 2-phenyl-2-butanol and shift differences for enantiomers were observed in each case (0.02 ppm for the α-methyl resonance for 2-butanol and 0.04 ppm for the α-methyl resonance for 2-phenyl-2-butanol). However, shift differences were substantially smaller than those observed with the more readily available facam and hfbc chelates.

Pirkle and coworkers have developed a similar direct nmr method based on chemical-shift nonequivalence of enantiomers in optically active solvents.[10] An important feature of their technique is that enantiomeric configurations can be correlated with chemical shift differences and thus absolute configurations can be established.[10b] However, the method is limited to polar solvent–solute combinations because nonequivalence results from diastereomeric solute–solvent interactions. Also, shift differences tend to be small ($\leq$0.04 ppm),[10] which limits the usefulness of this technique for determining enantiomeric purities. On the other hand, we have observed shift differences of >1 ppm for enantiotopic protons with facam and hfbc lanthanide chelates and these reagents are applicable to those classes of compounds that respond to conventional nmr shift reagents.

In a parallel study Whitesides and Lewis have investigated a number of chiral nmr shift reagents which can be represented by structure I where R is derived from optically active fencholic acid and structure II where R and R′ are derived from *d*-campholic acid or active fencholic acid.[3b,11] Comparison of their results with ours indicates that tris(*d*,*d*-dicampholylmethanato)europium(III), $Eu(dcm)_3$, induces larger shift differences for enantiomers than those observed with $Eu(facam)_3$ and $Eu(hfbc)_3$. $Eu(dcm)_3$ appears to be especially useful for substrates in which the chiral center is far from the site of coordination. However, these reagents are more difficult to prepare than the fluorinated acyl camphor chelates, and thus the latter appear to be more convenient for routine use.

Direct determination of enantiomeric purities with optically active nmr shift reagents[3-6,12] has obvious advantages over the indirect nmr method developed by Mislow and coworkers[13] and modified and refined by others.[14] This method involves derivatization of a chiral compound with an optically pure reagent and determining the diastereomeric composition of the derivative (which barring racemization or diastereoisomeric fractionation corresponds to the enantiomeric composition of the original sample) by nmr analysis.[13] An original shortcoming of the method, small shift differences for diastereotopic protons,[13,15] is largely eliminated by use of nmr lanthanide shift reagents.[14b,16] However, at best the method is laborious and limited to those compounds that can be derivatized with an optically pure reagent without racemization or iso-

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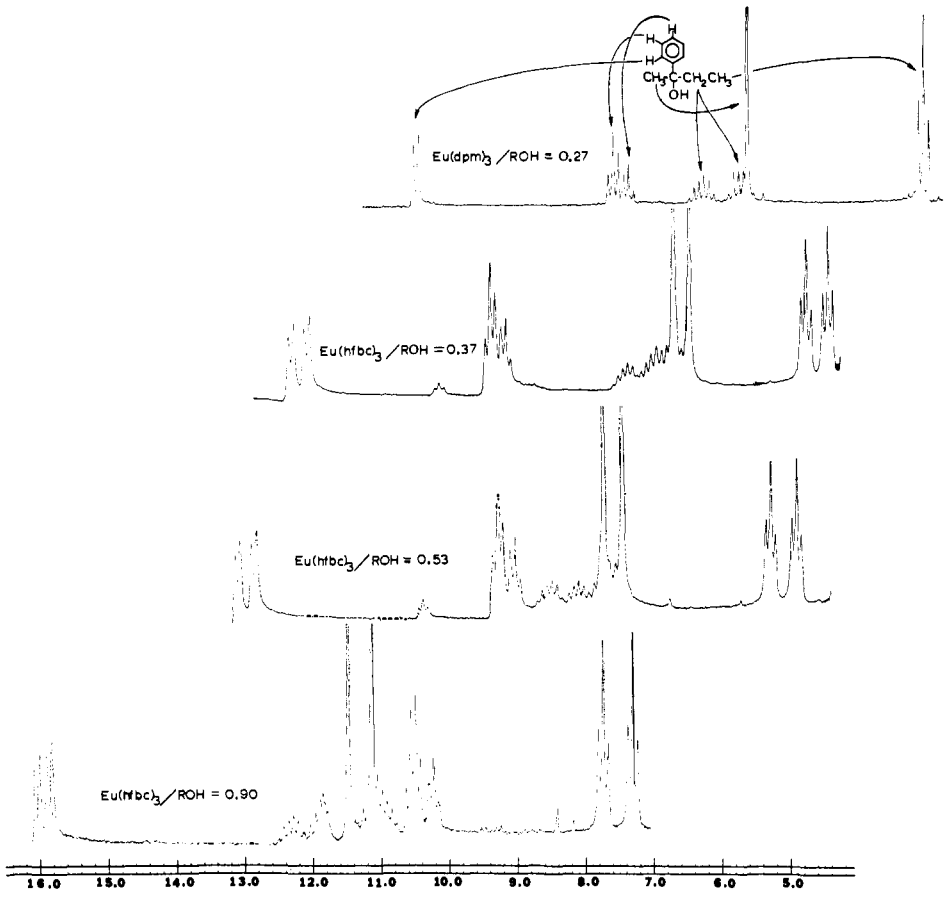

Figure 1. Spectra of *dl*-2-phenyl-2-butanol in CCl_4 in (a) the presence of 0.1 *M* $Eu(dpm)_3$ (upper spectrum) and (b) the presence of 0.2 *M* $Eu(hfbc)_3$ at three different $Eu(hfbc)_3$–substrate molar ratios.

meric fractionation. It is noteworthy that this method has recently been shown to be useful for correlation of optical configurations.[14a]

Our preliminary report[4] outlined the general applicability of $Eu(facam)_3$ for determination of enantiomeric compositions. Figure 1 shows spectra of *dl*-2-phenyl-2-butanol in the presence of $Eu(hfbc)_3$ at various shift-reagent–substrate molar ratios and in the presence of tris(dipavaloylmethanato)europium(III), $Eu(dpm)_3$ (upper spectrum). With the optically active shift reagent the enantiomers have nonequivalent spectra, and resonances for the enantiotopic α- and β-methyl protons and ortho protons are completely separated. The β-methyl (triplet) and ortho-proton (doublet) resonances for the enantiomers can be selectively spin decoupled. Two factors to be considered in discussing the effects of the optically active shift reagents on the nmr spectra of chiral substrates are (a) magnitudes of induced shifts ($\Delta\delta$) and (b) magnitudes of chemical-shift differences (nonequivalence) for enantiotopic nuclei ($\Delta\Delta\delta$). As shown by the lower three spectra in Figure 1, the induced downfield shift ($\Delta\delta$) increases with shift-reagent–substrate molar ratio as would be expected for a lanthanide shift reagent.[17] However, as will be illustrated later, enantiomeric shift differences ($\Delta\Delta\delta$) are complicated (and unpredictable) functions of the molar ratio.

All data in our earlier report, and in this paper, are for carbon tetrachloride solutions. Magnitudes of induced shifts ($\Delta\delta$) and of enantiomeric shift differences

(17) B. C. Mayo, *Chem. Soc. Rev.*, 2, 49 (1973).

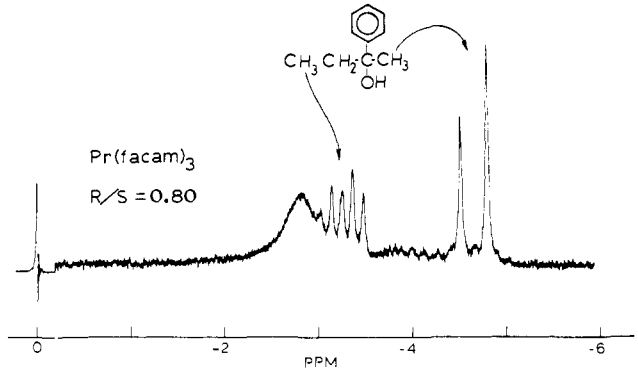

Figure 2. Upfield portion of the spectrum of partly resolved (excess *R* enantiomer) 2-phenyl-2-butanol in CCl_4 in the presence of 0.3 *M* $Pr(facam)_3$.

($\Delta\Delta\delta$) in the presence of the facam and hfbc chelates are larger in carbon tetrachloride than in deuteriobenzene or chloroform. These observations are consistent with an earlier report that magnitudes of spectral nonequivalence for enantiomers resulting from diastereotopic interactions between a chiral alcohol and optically active sulfoxides are larger in carbon tetrachloride than in chloroform.[18]

The effect of $Pr(facam)_3$ on the spectrum of partly resolved 2-phenyl-2-butanol is shown in Figure 2. In this case the shift is in the upfield direction. The broad resonance centered at -2.8 ppm is due to the shift

(18) F. A. L. Anet, L. M. Sweeting, T. A. Whitney, and D. J. Cram, *Tetrahedron Lett.*, 2617 (1968).

Table I. Shift Differences ($\Delta\Delta\delta$) for Enantiotopic Protons in the Presence of Eu(facam)$_3$ and Eu(hfbc)$_3$[a]

Compd	Proton	——$\Delta\Delta\delta$, ppm—— Eu-(facam)$_3$	Eu(hfbc)$_3$
2-Butanol	α-CH_3	0.08	
2-Butyl acetate	α-CH_3	0.23	
dl-Menthol	4-CH_3	0.07	
dl-Menthyl acetate[b,c]	4-CH_3	0.25	
1-Phenylethanol	α-H	0.37	0.40
	α-CH_3	0.00	0.22
1-Phenylethyl acetate	α-CH_3	0.18	
1-Phenylethyl *o*-methylbenzoate	α-CH_3	0.08	
	o-CH_3	0.03	
2-Methoxy-2-phenylbutane	O-CH_3	0.00	0.02
Methyl mandalate	α-H	0.17	
	O-CH_3	0.07	
α-Methyl-γ-phenylallyl *p*-nitrobenzoate	α-CH_3	0.18	
α-Phenyl-γ-methylallyl acetate	γ-CH_3	0.18	
	OAc	0.10	
Dimethyl *trans*-1,2-cyclobutanedicarboxylate	O-CH_3	0.02	0.05
2-Phenyl-2-butanol[d]	α-CH_3	0.31	0.55
	β-CH_3	0.21	0.17
	o-H	0.12	0.28
Methyl 2-methyl-2-phenylbutanoate	O-CH_3	0.12	0.22
	α-CH_3	0.05	0.13
	β-CH_3	0.05	0.20
3-Methyl-3-phenyl-2-pentanone	$COCH_3$	0.13	0.13
	α-CH_3	0.10	0.10
	β-CH_3	0.02	0.00
2-Methyl-*endo*-norbornanol	2-CH_3	0.20	
Norbornyl acetate	$COCH_3$	0.15	
2-Benzonorbornenone	1-H		0.32
1-Methyl-2-norbornanone	1-CH_3	0.17	
1-Methyl-2-benzonorbornenone	1-CH_3	0.15	0.43
2-Methyl-*endo*-2-benzonorbornenol	2-CH_3	0.03	0.37
1,2-Dimethyl-*exo*-2-benzonorbornenol[e]	1-CH_3	0.60	0.24
	2-CH_3	0.38	0.08
6,7-Dimethoxy-*exo*-2-benzonorbornenol[e]	6-OCH_3	0.00	
	7-OCH_3	0.08	
2-Amino-3,3-dimethylbutane	α-H	0.40	0.12[e]
	α-CH_3	0.22	0.20[e]
	β-CH_3	0.03	0.13[e]
1-Phenylethylamine	α-H	0.92	0.22[e]
	α-CH_3	0.18	0.17[e]
Methyl phenyl sulfoxide[e]	CH_3		0.07
2-Octyl phenyl sulfone[e]	α-CH_3		0.24
1-Adamantyl 4-(1-pentenyl) sulfone[e]	CH_3		0.40
α-Deuteriobenzyl alcohol	α-H	*f*	0.28
Benzyl alcohol	α-H[g]	*f*	0.28
2-Propanol[e]	CH_3[g]	*f*, *h*	0.10
Dimethyl sulfoxide	CH_3[g]	*f*, *h*	0.10[e]
Dibenzyl sulfoxide	CH_2[g]	0.08	0.12[e]
Dibenzyl sulfone	CH_2[g]	0.00	0.19[e]
Phenyl 1-(3-methyl-2-butenyl) sulfone[e]	α-H[g]	*f*	0.78

[a] Except as noted spectra obtained with a 60-MHz instrument. The solvent was CCl_4 and shift reagent concentrations were 0.2–0.3 *M*. Shift-reagent substrate molar ratios were in the range 0.5–1.0 for Eu(facam)$_3$ and 1.0 to 2.0 for Eu(hfbc)$_3$. [b] Mole ratio 1.5. [c] Spectra obtained with a 100-MHz instrument; concentrations about half those used for 60-MHz spectra. [d] Relative magnitudes of shift differences for three sets of enantiotopic protons sensitive to shift-reagent–substrate ratio. See Figure 6. [e] Mole ratio in the range 0.4 to 0.6. [f] Resonance broadened and featureless. [g] Protons enantiotopic by internal comparison. [h] Small shift differences for these cases have recently been reported (ref 21).

reagent. The resolution of the α- and β-methyl proton signals is about the same (2 Hz at one-half peak height) as that observed with the europium analog.[4] However, the aromatic proton absorption (downfield from TMS and not shown) is broad and lacking of fine structure. In other cases we have similarly observed poorer resolution of certain signals with the optically active praseodymium chelates than with the corresponding europium analogs.

Additional data demonstrating the generality of nmr spectral nonequivalence of enantiomers in the presence of Eu(facam)$_3$ and Eu(hfbc)$_3$ are presented in Table I. This table shows shift differences ($\Delta\Delta\delta$) for the indicated enantiotopic protons in the presence of the two shift reagents. The praseodymium chelates have also been investigated with several of the compounds. Induced shifts ($\Delta\delta$) are larger and usually, but not always, $\Delta\Delta\delta$ is also larger with the praseodymium chelates than with the europium chelates.

Magnitudes of shifts induced by Eu(facam)$_3$ and Eu(hfbc)$_3$ increase with the reagent/substrate molar ratio up to a point and then tend to level off at higher ratios. Similar behavior has been observed with tris(1,1,1,2,2,3,3-heptafluoro-7,7-dimethyl-4,6-octanedionato)europium(III), Eu(fod)$_3$.[19,20] At a fixed molar ratio $\Delta\delta$ is rather insensitive to change in concentration.[20] Thus, it is straightforward to predict molar ratios for a large, if not maximum, $\Delta\delta$. However, conditions for a maximum, or suitably large $\Delta\Delta\delta$, are not readily predictable because magnitudes of nonequivalence are complicated functions of the reagent–substrate ratio and, unlike $\Delta\delta$, $\Delta\Delta\delta$ may pass through a maximum and close (and even reverse the sense of nonequivalence) as the molar ratio is increased. Also, $\Delta\Delta\delta$ for different sets of enantiotopic protons in a molecule may vary independently as the molar ratio (and $\Delta\delta$) is increased. Thus, the best conditions for separating one set of enantiotopic resonances will not necessarily be the best conditions for other sets of enantiotopic resonances in the same spectrum.

For the above reasons the observed values of $\Delta\Delta\delta$ in Table I are not necessarily the largest obtainable; conditions were optimized in only a few cases. Molar ratios for these data were generally in the range producing large induced shifts and large shift differences for enantiotopic signals. In cases where the effect of varying the reagent–substrate molar ratio was investigated, the ratio was varied by successive additions of substrate to a solution of the shift reagent in carbon tetrachloride (*i.e.*, the spectrum at the highest ratio was determined first). At a fixed molar ratio, $\Delta\Delta\delta$ (like $\Delta\delta$)[20] is quite insensitive to change in concentration and tends to increase slightly with a decrease in concentration.

The general applicability of the facam and hfbc chelates for determination of enantiomeric compositions is demonstrated by the data in Table I and has been substantiated by other work.[5,6,12,21] The hfbc chelates induce larger shifts than the facam chelates

(19) R. E. Rondeau and R. E. Sievers, *J. Amer. Chem. Soc.*, **93**, 1522 (1971).

(20) B. I. Shapiro and M. D. Johnston, Jr., *J. Amer. Chem. Soc.*, **94**, 8185 (1972).

(21) It has also been shown that Eu(facam)$_3$ can sometimes be used to distinguish between *meso* and *dl* diastereoisomers: M. Kainosho, K. A. Jisaka, W. H. Pirkle, and S. B. Beare, *J. Amer. Chem. Soc.*, **94**, 5924 (1972).

and as the data in the table show, in most cases $\Delta\Delta\delta$ is also larger with Eu(hfbc)$_3$ than with Eu(facam)$_3$. However, there are notable exceptions. In the case of amines, larger shift differences are observed with the facam chelates. Similarly, $\Delta\Delta\delta$ is appreciably larger for both methyl groups of 1,2-dimethyl-*exo*-2-benzonorbornenol with Eu(facam)$_3$ than with Eu(hfbc)$_3$. With the other benzonorbornenyl derivatives in the table, Eu(hfbc)$_3$ is clearly more effective than Eu(facam)$_3$ for separating enantiotopic resonances.

The most pronounced (and consistent) difference between the facam and hfbc chelates is with prochiral substrates in which protons are enantiotopic by internal comparison[22] (last six entries in Table I). In every case investigated nonequivalence was observed with Eu(hfbc)$_3$, whereas with Eu(facam)$_3$, nonequivalence was observed only with dibenzyl sulfoxide. Spectral nonequivalence of protons enantiotopic by internal comparison in the presence of Eu(hfbc)$_3$ has also been observed by Fraser and coworkers.[5b]

Complete separation of at least one set of enantiotopic resonances is a necessary, but not sufficient, requirement for direct determination of enantiomeric compositions from relative peak areas. It is also necessary to avoid overlap of the separated resonances with other signals. In nearly every case that we have investigated we have been able to isolate and separate at least one set of enantiotopic resonances with one of the hfbc or facam chelates. Isolation of separated enantiotopic signals from other resonances can sometimes be achieved by changing from the europium to praseodymium chelate. No single reagent is superior to the others for every application.

In many cases any of the four chelates give suitable spectra for direct determination of enantiomeric compositions over a considerable range of reagent–substrate molar ratios. In other cases conditions are more restricted and several experiments may be required to determine conditions for obtaining useful spectra. In this connection it should be noted that the limited data in Table I suggests that conversion of an alcohol to the acetate increases $\Delta\Delta\delta$. This also introduces an additional methyl singlet that may be a useful spectral feature (the enantiotopic acetyl methyl protons in some acetates have nonequivalent resonances in the presence of the active shift reagents). Thus, in some cases derivatization may facilitate determination of enantiomeric compositions.

The effect of Eu(hfbc)$_3$ on the spectrum of ethyl propionate is about the same (for all protons in the molecule) as that reported for Eu(fod)$_3$;[19] plots of $\Delta\delta$ *vs.* molar ratio for the two shift reagents are virtually superimposed. Eu(facam)$_3$ induces shifts that are only about one-third as large. The effects of Eu(hfbc)$_3$, Eu(fod)$_3$, and Eu(facam)$_3$ on the spectrum of *dl*-2-phenyl-2-butanol at different reagent–substrate molar ratios are shown in Figure 3. In the presence of the optically active reagents the enantiomers have nonequivalent spectra (see Figures 1 and 2) and values of $\Delta\delta$ used in the plots are averages (midpoints) of the shifts for the enantiotopic resonances. The $\Delta\delta$ values for the β-methyl and ortho protons showed similar relative efficiencies for the three reagents.

In Figure 3, the shape of the plot for Eu(facam)$_3$

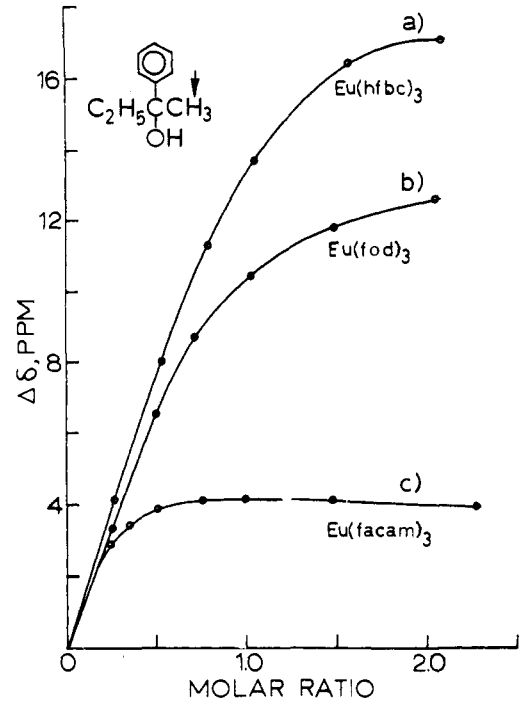

Figure 3. Plot of $\Delta\delta$ *vs.* shift-reagent–substrate molar ratio for the designated methyl protons of *dl*-2-phenyl-2-butanol in the presence of (a) 0.3 *M* Eu(hfbc)$_3$, (b) 0.3 *M* Eu(fod)$_3$, and (c) 0.4 *M* Eu(facam)$_3$.

differs from that for Eu(hfbc)$_3$ in a way that suggests that the stoichiometry and/or binding constants for coordination differ for the two reagents. With Eu(facam)$_3$, $\Delta\delta$ reaches a plateau at a molar ratio of a little over 0.5 and then declines gradually at higher molar ratios; similar behavior was observed with other substrates. On the other hand, with Eu(fod)$_3$ and Eu(hfbc)$_3$, $\Delta\delta$ increases over the range investigated. The shapes of the curves suggest that Eu(facam)$_3$ forms a 1:2 reagent:substrate complex (presumably by a two-step mechanism[20]) with high binding constants; at molar ratios <0.5 all of the substrate is evidently complexed and the nmr spectrum is that of the complex. The slight decline in $\Delta\delta$ at higher ratios suggests involvement of a monocoordinated species which has a smaller downfield shift than the 1:2 complex. The curves for Eu(hfbc)$_3$ and Eu(fod)$_3$ indicate that monocoordination is involved with binding constants such that mole ratios of >2 are required for complete coordination. However, as will be shown later, this interpretation is an oversimplification in the case of Eu(hfbc)$_3$ because at least two complexes are involved and the relative amounts of these vary with the molar ratio.

Plots of $\Delta\delta$ *vs.* molar ratio for several substrates in the presence of Eu(facam)$_3$ are shown in Figure 4, and similar plots for Eu(hfbc)$_3$ are shown in Figure 5. These plots show that in general Eu(facam)$_3$ evidently forms a 1:2 complex with high binding constants; $\Delta\delta$ reaches a maximum value at a molar ratio of between 0.5 and 1. The plot for 2-amino-3,3-dimethylbutane closely approximates the intersecting dashed lines which represent a hypothetical case involving complete dicoordination and a chemical shift of 10 ppm for the 1:2 complex. With Eu(hfbc)$_3$, binding constants are lower and in general $\Delta\delta$ increases up to a molar ratio of <2. Similar behavior was observed with other substrates

(22) M. Raban and K. Mislow, *Top. Stereochem.*, 1, 1 (1967).

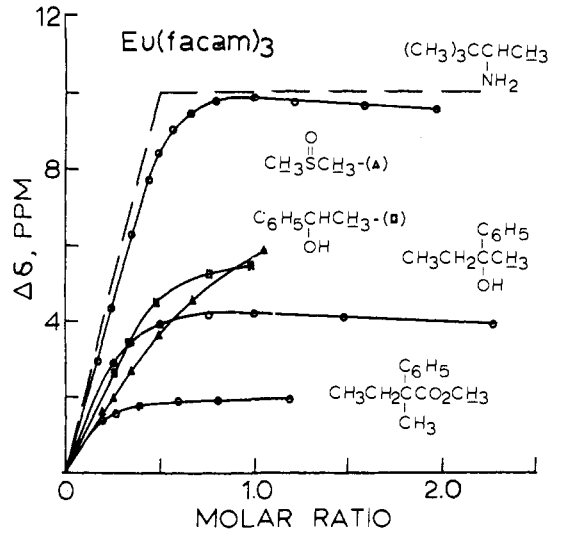

Figure 4. Plots of $\Delta\delta$ *vs.* molar ratio for the designated protons of the various compounds in the presence of 0.3 *M* Eu(facam)$_3$. The intersecting dashed lines represent a hypothetical case involving the formation of a 1:2 reagent–substrate complex assuming no dissociation and a chemical shift of 10 ppm for the complex.

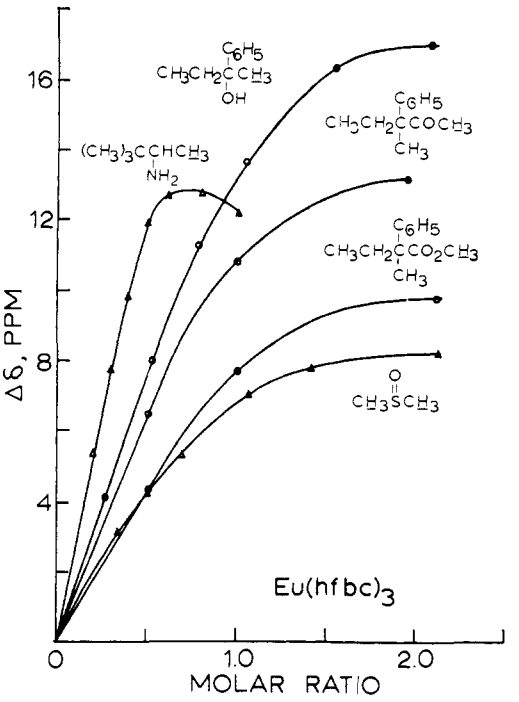

Figure 5. Plots of $\Delta\delta$ *vs.* molar ratio for the designated protons of the various compounds in the presence of 0.3 *M* Eu(hfbc)$_3$.

not included in Figures 4 and 5. From these plots it can be seen that, in general, favorable molar ratios for large induced shifts ($\Delta\delta$) are 0.5 to 1 for Eu(facam)$_3$ and <1 for Eu(hfbc)$_3$. Shift differences for enantiotopic resonances ($\Delta\Delta\delta$) are also usually large over these ranges.

Two exceptions to the above generalities are the behavior of dimethyl sulfoxide in the presence of Eu(facam)$_3$ (Figure 4) and the effect of Eu(hfbc)$_3$ on 2-amino-3,3-dimethylbutane (Figure 5); 1-phenylethylamine gave a similar plot. It appears that these exceptions result from atypical coordination. Evidently dimethyl sulfoxide, unlike the other substrates in Figure 4 and several others that were investigated, forms a 1:1 complex with Eu(facam)$_3$. The anomalous behavior of the amine in the presence of Eu(hfbc)$_3$ clearly shows that at least two coordinated species are involved. Apparently dicoordination with high binding constants gives a species with large downfield shifts. At higher molar ratios this is replaced by a different species (presumably a 1:1 complex) with smaller downfield shifts. Thus, $\Delta\delta$ passes through a maximum. Another unusual thing about these two cases is that above a molar ratio of 1, broadening of signals becomes excessive and useful spectra could not be obtained. For this reason, these two plots could not be extended to higher molar ratios.

In our earlier report[4] we noted that in the spectrum of 3-methyl-3-phenyl-2-pentanone in the presence of Eu(facam)$_3$ the sense of nonequivalence is not the same for all sets of enantiotopic protons. Similar behavior is observed with Eu(hfbc)$_3$. The acyl–methyl resonance for the *R* enantiomer is shifted more than that for the *S* enantiomer, whereas the situation is reversed for the α-methyl and β-methyl signals. Similarly, in the spectrum of methyl 2-methyl-2-phenylbutanoate in the presence of the facam or hfbc chelates, senses of nonequivalence are reversed for the β-methyl and O-methyl resonances. As was pointed out,[4] different senses of nonequivalence in a spectrum clearly show that induced shift differences for enantiomers is not simply a matter of different equilibrium constants for coordination of the enantiomers; in this case the spectrum of the enantiomer complexed to the greatest extent would be shifted the most and senses of nonequivalence would be the same for all separated enantiotopic resonances.

The dependence of magnitudes of nonequivalence ($\Delta\Delta\delta$) on the reagent–substrate molar ratio (*i.e.*, degree of coordination) also suggests that nonequivalence is not primarily due to different binding constants for enantiomers. In this case $\Delta\Delta\delta$ would pass through a maximum at low molar ratios and close as coordination became complete. However, this is not the general pattern. Inspection of spectra that provided the data for Figures 3–5 reveals a diversity of results. For most of the substrates in the presence of Eu(facam)$_3$ values of $\Delta\Delta\delta$ for at least one set of enantiotopic protons tend to increase with increasing coordination up to complete coordination (at molar ratios where $\Delta\delta$ remains steady). However, $\Delta\Delta\delta$ values for different sets of enantiotopic resonances vary independently and $\Delta\Delta\delta$ for some signals may pass through maxima and decline while others increase with increasing coordination. Only in the cases of 2-amino-3,3-dimethylbutane and α-phenylethylamine in the presence of Eu(hfbc)$_3$ did maxima $\Delta\Delta\delta$ values occur for all enantiotopic protons prior to the occurrence of maxima $\Delta\delta$. This could result from different binding constants for the enantiomers. However, it should be noted that in these cases $\Delta\delta$ *vs.* molar ratio plots are abnormal (see plot for 2-amino-3,3-dimethylbutane in Figure 5) and $\Delta\delta$ clearly does not parallel the degree of coordination.

In cases where several sets of enantiotopic protons were clearly distinguished, curious behavior was observed which is most dramatically illustrated by Figure 6 which shows plots of $\Delta\Delta\delta$ *vs.* molar ratio for three sets of enantiotopic resonances in the spectrum of 2-phenyl-2-butanol in the presence of Eu(hfbc)$_3$. It

Table II. Enantiotopic Protons Showing Largest Shifts in the Presence of Eu(facam)$_3$, Eu(hfbc)$_3$, Pr(facam)$_3$, and Pr(hfbc)$_3$[a]

Substrate	Proton	Shift reagent: Eu(facam)$_3$	Pr(facam)$_3$	Eu(hfbc)$_3$	Pr(hfbc)$_3$
2-Phenyl-2-butanol	α-CH_3	*R*	*R*	*R*	
	β-CH_3	*R*	*R*	*R*	
	o-H	*R*	*b*	*S*	
Methyl 2-methyl-2-phenylbutanoate	O-CH_3	*R*	*R*	*R*	
	α-CH_3	*R*	*R*	*R*	
	β-CH_3	*S*	*b*	*S*	
3-Methyl-3-phenyl-2-pentanone	$COCH_3$	*R*	*R*	*R*	*R*
	α-CH_3	*S*	*S*	*S*	*S*
	β-CH_3	*S*	*b*	*b*	*b*

[a] Conditions are those described in Table I. [b] Shift differences not observed or resonances broad and featureless.

should be noted that the degree of coordination, as reflected by $\Delta\delta$ for all protons, is increasing throughout the range of molar ratios.

The most striking feature of Figure 6 is the different behavior of each set of enantiotopic protons. The α-methyl resonances show increasing separation with increasing molar ratio (coordination) over the entire range whereas $\Delta\Delta\delta$ values for the β-methyl triplet pass through a maximum and then decrease and level off. Most remarkable of all is the plot for the ortho protons. In this case $\Delta\Delta\delta$ passes through a maximum at a molar ratio of *ca.* 0.5 and then closes and opens again at higher molar ratios with the sense of nonequivalence reversed. This reversal in the sense of nonequivalence was established with partly resolved 2-phenyl-2-butanol in which case the ortho-proton signals for the major and minor enantiomers crossed as the molar ratio was varied from 0.6 to 1.5. Three spectra from which data were taken for Figure 6 are shown in Figure 1. Inspection of these spectra shows that over this limited molar ratio range, $\Delta\delta$ for all protons increases with molar ratio and $\Delta\Delta\delta$ increases for the α-methyl singlet and β-methyl triplet but decreases for the ortho-proton doublet.

The effect of molar ratio on $\Delta\Delta\delta$ and the sense of nonequivalence show that with 2-phenyl-2-butanol in the presence of Eu(hfbc)$_3$ at least two coordinated species are involved; presumably a 1:2 complex predominates at low molar ratios and this is replaced by a 1:1 complex at higher molar ratios. These complexes have strikingly different chemical shift differences for the coordinated enantiomers and consequently $\Delta\Delta\delta$ changes dramatically for some resonances (even in sign for the ortho-proton signals) as the populations of the complexes change.

Inconsistencies in the sense of nonequivalence in the same spectrum and the behavior of $\Delta\Delta\delta$ as molar ratio (degree of coordination) is varied suggest that spectral nonequivalence for enantiomers has more to do with structural features of reagent–substrate complexes than with equilibrium constants for coordination. Magnitudes of lanthanide induced shifts are sensitive to the distance and orientation of the resonating nucleus with respect to the paramagnetic center.[17,23] Different $\Delta\Delta\delta$ values for 1:2 and 1:1 reagent–substrate complexes indicate different conformations and locations of the coordinated enantiomers and thus different relative orientations and distances for the enantiotopic protons.

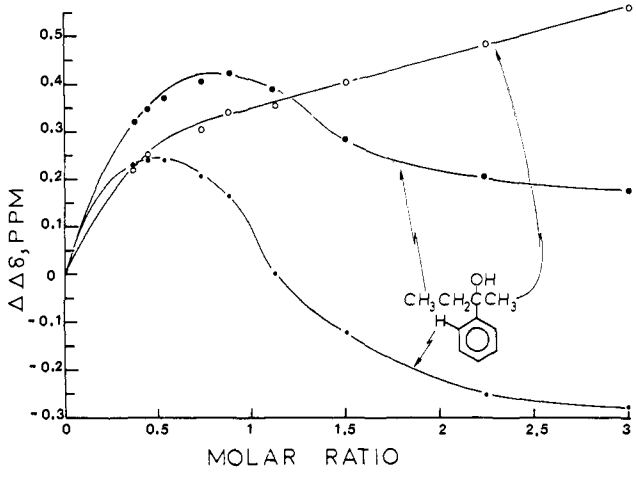

Figure 6. Plots of $\Delta\Delta\delta$ *vs.* molar ratio for the designated protons of 2-phenyl-2-butanol in the presence of 0.3 *M* Eu(hfbc)$_3$.

From the complex nature of factors responsible for enantiomeric shift differences, it appears that it will be very difficult to devise stereochemical models that will correlate senses of nonequivalence with absolute configurations. However, there is a remarkable consistency in the senses of nonequivalence induced by the facam and hfbc chelates. As shown in Table II, with one exception the same enantiotopic protons in a substrate undergo the largest induced shifts regardless of shift reagent or direction of the shift. The exception is the ortho protons of 2-phenyl-2-butanol in the presence of Eu(hfbc)$_3$ and, as has been noted, in this case the sense of nonequivalence depends on the molar ratio (Figure 6). At low molar ratios (<1) the doublet for the *R* enantiomer is downfield from that for the *S* enantiomer and the inconsistency vanishes. The data in Table II indicate that relative locations, orientations, and conformations of coordinated enantiomers are similar for the four chiral shift reagents.

In our earlier report[4] we noted that spectral nonequivalence is not observed for 2-propanol and dimethyl sulfoxide in the presence of Eu(facam)$_3$.[24] These substrates have methyl groups that are enantiotopic by internal comparison[22] and would be expected to become diastereotopic and thus anisochronous when coordinated with a chiral shift reagent. As can be seen from the last several entries in Table I, spectral non-

(23) W. D. Horrocks, Jr., J. P. Sipe, III, *J. Amer. Chem. Soc.*, **93**, 6800 (1971); P. V. Demarco, T. K. Elzey, R. B. Lewis, and E. Wenkert, *ibid.*, **92**, 5734 (1970); B. L. Shapiro, J. R. Hlubucek, G. R. Sullivan and L. F. Johnson, *ibid.*, **93**, 3281 (1971).

(24) It has recently been reported that spectral nonequivalence is observed in these cases as well as with 2-propylamine and 2-methyl-2-butanol (ref 21).

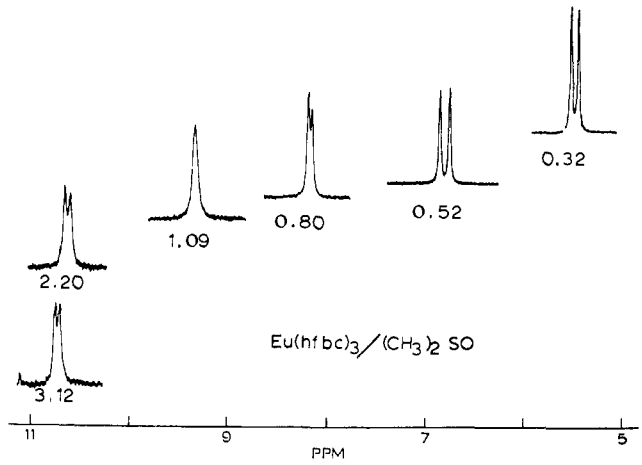

Figure 7. Spectra of dimethyl sulfoxide in CCl_4 in the presence of 0.3 *M* Eu(hfbc)$_3$. The reagent–substrate molar ratios are shown under each spectrum.

equivalence of protons that are enantiotopic by internal comparison can indeed be observed in many cases.

With benzyl alcohol in the presence of 2 equiv of Eu(hfbc)$_3$ the signal for the α protons is an AB quartet. The geminal protons have a coupling constant of 13 Hz and a shift difference of 0.28 ppm. Similar results have been observed in a parallel investigation.[5b] It is interesting to note that $\Delta\Delta\delta$ induced by Eu(hfbc)$_3$ is the same for benzyl alcohol (protons enantiotopic by internal comparison) as for deuteriobenzyl alcohol (protons enantiotopic by external comparison). This indicates that, as would be expected, replacement of hydrogen by deuterium has no effect on the location, conformation, or orientation of the coordinated substrate.

For substrates with only a prochiral[22] center, spectral nonequivalence of enantiotopic protons cannot result from different binding constants. In these cases shift differences must result from conversion of enantiotopic protons to diastereotopic protons by coordination with the chiral shift reagent. It is interesting to note that with these substrates magnitudes of nonequivalence also vary with the reagent–substrate molar ratio in unpredictable ways.

Figure 7 shows spectra of dimethyl sulfoxide in the presence of Eu(hfbc)$_3$ at varying molar ratios. The important feature of this figure is the change in magnitudes of nonequivalence with molar ratio. Initially, increasing the reagent–substrate ratio causes an increase in $\Delta\Delta\delta$. At a molar ratio of 0.5, $\Delta\Delta\delta$ reaches a maximum and then starts to close and nonequivalence vanishes at a ratio of 1. Further increase in the ratio restores nonequivalence (presumably with reversal in the sense of nonequivalence). It should be noted that up to a molar ratio of 2.2, coordination increases as indicated by the increase in $\Delta\delta$; evidently essentially all of the substrate is coordinated above a molar ratio of 2.2.

Here again there is evidence that at least two coordinated species are involved and the sense of nonequivalence differs for the complexes. The simplest explanation is that at low molar ratios a 1:2 reagent–substrate complex predominates and that at higher ratios a 1:1 complex predominates. The locations and orientations of the coordinated substrate in the two complexes are such that the enantiotopic methyl that is shifted the most in one complex is shifted the least in the other.

Experimental Section

General. Boiling points and melting points are uncorrected. Nuclear magnetic resonance spectra were obtained with a Varian A-60-A, HA-100, or XL-100 spectrometer. Chemical shift values are expressed as δ (parts per million) relative to TMS as an internal standard. Optical rotations were determined with a Perkin–Elmer Model 141 polarimeter. Elemental analyses were performed by Galbraith Laboratories, Inc., Knoxville, Tenn. *d*-Camphor, mp 178°, $[\alpha]^{20}D$ 41.3° (*c* 4.9, ethanol), was obtained from Eastman Kodak Co. The sodium hydride was a 59.5% dispersion in mineral oil. Dimethoxyethane was distilled from sodium hydride before use. Substrates listed in Table I that are not described below were commercial samples or were prepared (and in some cases resolved) by methods described in the literature.

Preparation of (R,R)-3,7-Dimethyl-3,7-diphenyl-4,6-nonanedione. Optically pure (*R*)-(−)-2-methyl-2-phenylbutanoic acid, $[\alpha]^{25}D$ −29.6° (*c* 4.9, benzene) [lit.[8a] $[\alpha]^{25}D$ −29.2° (*c* 4.8, benzene)], was converted to *R*-(−)-methyl 2-methyl-2-phenylbutanoate [bp 123–125° (17 mm); $[\alpha]^{25}D$ −18.85° (neat, 1 dm) (lit.[8c] $[\alpha]^{26}D$ −19.23° (neat, 1 dm))] by a previously reported procedure. The nmr and ir spectra of the acid and ester were indistinguishable from those for authentic racemic samples. The above described optically active acid was also converted to (*R*)-(−)-3-methyl-3-phenyl-2-pentanone by a reported procedure.[8a] The optically active ketone had bp 120–121° (18 mm); $[\alpha]^{28}D$ −66.2° (neat, 1 dm) [lit.[8a] $[\alpha]^{23}D$ −70.3° (neat, 1 dm)]. The nmr and ir spectra of the ketone were indistinguishable from those for an authentic racemic sample.

The optically active β-diketone was prepared by condensation of the above described (*R*)-(−)-3-methyl-3-phenyl-2-pentanone and (*R*)-(−)-methyl 2-methyl-2-phenylbutanoate by the procedure outlined below which is based on a general method.[9] A solution of 2.78 g (15.8 mmol) of ketone in 10 ml of dimethoxyethane was added dropwise over a period of 30 min to a refluxing solution of 2.88 g (15.0 mmol) of the ester and 2 g (50 mmol) of sodium hydride in 30 ml of dimethoxyethane. After gas evolution ceased, the reaction mixture was cooled and stirred overnight. The reaction mixture was carefully acidified with hydrochloric acid and extracted with four 15-ml portions of ether. The combined ether extracts were shaken with aqueous sodium bicarbonate and brine. Evaporation of the solvent and distillation of the residual oil gave 2.08 g (59%) of colorless (*R,R*)-(−)-3,7-dimethyl-3,7-diphenyl-4,6-nonanedione: bp 152–164° (0.3 mm); $[\alpha]^{25}D$ −26.4° (*c* 3.0, benzene); nmr (CCl_4) δ 0.78 (t, 6 H), 1.40 (s, 6 H), 1.96 (m, 4 H), 3.06 (s, 0.4 H), 5.34 (s, 0.8 H), 7.26 (s, 10 H), 11.46 (s, 0.8 H).

3-Trifluoroacetyl-*d*-camphor. In a typical preparation 30.4 g (0.20 mol) of *d*-camphor was added to a mixture of 19 g (0.47 mol) of sodium hydride in 300 ml of dimethoxyethane. The mixture was refluxed for 1 hr under nitrogen after which a solution of 31.3 g (0.22 mol) of ethyl trifluoroacetate in 100 ml of dimethoxyethane was added over a period of 1.5 hr. Gas was evolved during the addition of the ester. Reflux was continued for 2 hr after which the reaction mixture was cooled and 25 ml of ethanol was added to consume the excess sodium hydride. The deep red solution was poured into 600 ml of water, acidified with concentrated hydrochloric acid, and extracted with four 200-ml portions of pentane. The combined pentane extracts were washed with 5% sodium bicarbonate and water. After drying ($MgSO_4$) the extract was concentrated to 45.6 g of dark red liquid. The crude material was purified by chromatography on 800 g of silica gel (grade 950, 60–200 mesh, Grace-Davison Chemical Co.). The column was first eluted with 1750 ml of hexane to remove the mineral oil derived from the sodium hydride dispersion. The desired product was removed with 3200 ml of 5% ether in hexane. Emergence of the product coincided with the elution of a red band that probably results from the reaction of the product with traces of iron in the silica gel. The diketone gave an intense red color with a 1% ferric chloride solution. The product was further purified by distillation which gave 25.1 g (53% yield) of a colorless liquid: bp 100–101° (16 mm); ir (neat) 2700 (b, OH), 1698 (C=O), 1650 (C=C), 1145 and 1190 cm^{-1} (CF); nmr (CCl_4) δ 0.88 (s, 3 H), 1.00 (s, 6 H), 1.3–2.3 (m, 4 H), 2.90 (m, 1 H), 11.36 (s, 1 H); uv max (hexane) 266 mμ (ϵ 8290); $[\alpha]^{20}D$ 149° (*c* 2.4, CCl_4).

Anal. Calcd for $C_{12}H_{15}F_3O_2$: C, 58.06; H, 6.09. Found: C, 58.17; H, 6.09.[25]

3-Heptafluorobutyryl-*d*-camphor. This β-diketone was prepared by a procedure based on a previously reported method.[26] In a typical preparation a mixture of 9.2 g (0.24 mol) of sodium amide and 35.8 g (0.24 mol) of *d*-camphor in 300 ml of dimethoxyethane was refluxed under nitrogen until ammonia evolution ceased (about 2 hr). The stirred mixture was cooled to 10° and 18.2 g (0.08 mol) of heptafluorobutyryl chloride (Pierce Chemical Co.) in 50 ml of dimethoxyethane was added over a 30-min period. The reaction mixture was worked up as described above for the trifluoromethyl derivative.

The crude product (45.9 g) was dissolved in methanol and 300 ml of 0.3 *M* aqueous cupric acetate was added. A dark green oil separated and the mixture was stirred 0.5 hr and extracted with pentane. The pentane extract was washed with water and sodium bicarbonate and dried over sodium sulfate. Evaporation of the solvent gave 49 g of a residual dark green oil. The excess camphor was removed by heating overnight at 70° under reduced pressure (<0.1 mm). The diketone was regenerated from the copper chelate by adding 100 ml of ether and shaking the resulting solution with 200 ml of 10% sulfuric acid. The aqueous layer was extracted with ether and the combined ether extracts were washed with water, 5% sodium bicarbonate, and brine, dried over magnesium sulfate, and concentrated to 22.0 g of dark red liquid. The crude product was distilled to give 17.4 g (64.0% yield) of a colorless liquid: ir (neat) 1698 (C=O), 1640 (C=C), 1227 cm^{-1} (C-F); nmr (CCl_4) δ 0.83 (s, 3 H), 0.96, 0.98 (two s, 6 H), 1.2–2.2 (m, 4 H), 2.78 (m, 1 H), 11.60 (s, 1 H); uv max (hexane) 267 mμ (ε 9250); $[\alpha]^{20}D$ 127° (*c* 2.6, CCl_4).

Anal. Calcd for $C_{14}H_{15}F_7O_2$: C, 48.28; H, 4.34. Found: C, 48.47; H, 4.53.

Tris(3-trifluoroacetyl-*d*-camphorato)europium(III), Eu(facam)$_3$. The chelated compounds were prepared by a previously reported method.[7] The preparation of Eu(facam)$_3$ will be described in detail as a typical example. Solutions of (a) 5.95 g (24.0 mmol) of 3-trifluoroacetyl-*d*-camphor in 24 ml of a 50% ethanolic solution of 1 *N* sodium hydroxide and (b) 2.94 g (8.00 mmol) of europium(III) chloride hexahydrate (99.99%, Rare Earth Division, American Potash and Chemical Corp., West Chicago, Ill.) in 25 ml of 95% ethanol were prepared. The $EuCl_3$ solution was clarified by adding a drop or two of concentrated hydrochloric acid and then the solution was added to the basic solution of the β-diketone. A bright yellow, resinous precipitate formed immediately. The mixture was stirred for 2 hr after which 50 ml of water was added and the stirring continued for an additional 0.5 hr. The resinous precipitate was taken up in pentane and the aqueous layer was extracted with pentane. The combined pentane extracts were washed with water, dried over magnesium sulfate, and filtered with coarse filter paper. The bright yellow, slightly turbid solution was clarified by filtration with Whatman's No. 2 paper. Evaporation of the pentane gave a glassy solid which was crushed and evacuated at 70° to 0.1 mm for several hours to give 5.88 g (82% yield) of a fine, yellow-orange powder: mp indefinite (remains a solid up to 120°); ir ($CHCl_3$) 1652 (C=O), 1540 cm^{-1} (C=C); nmr (CCl_4) δ 0.18, 0.33, 1.58, 2.58 (all resonances broad); uv max (hexane) 306 (ε 19,000), 274 mμ (sh, ε ~10,000); $[\alpha]^{20}D$ 173° (*c* 1.4, CCl_4).

Anal. Calcd for $C_{36}H_{42}F_9O_6Eu$: C, 48.38; H, 4.74. Found: C, 48.60; H, 4.72.

A sample of Eu(facam)$_3$ was distilled in the following manner. About 1 g was placed in a small sublimation apparatus. A plug of glass wool was inserted between the sample and a cold finger. The sample was distilled through the glass wool under reduced pressure (>0.1 mm) by partially submerging the apparatus in a Wood's-metal bath at 250°. Several solid fractions of sample were collected on the cold finger. This material had ir and nmr spectra indistinguishable from those for undistilled Eu(facam)$_3$ and performed no better as a chiral shift reagent.

Tris(3-heptafluorobutyryl-*d*-camphorato)eruopium(III), Eu(hfbc)$_3$. Following the standard procedure, to 10.46 g (30.0 mmol) of 3-heptafluorobutyryl-*d*-camphor dissolved in 29.7 ml of 1 *N* sodium hydroxide was added 3.66 g (10.0 mmol) of europium(III) chloride hexahydrate in 30 ml of ethanol. After stirring for 2 hr, the reaction mixture was worked up in the usual way to give 8.86 g (74% yield) of a yellow-orange powder: mp 158–165°; ir ($CHCl_3$) 1649 (C=O), 1526 cm^{-1} (C=C); nmr (CCl_4) δ 0.73, 2.25, 3.97 (all resonances broad); uv max (hexane) 310 (ε 23,760), 270 mμ (weak shoulder); $[\alpha]^{20}D$ 169° (*c* 1.3, CCl_4).

Anal. Calcd for $C_{42}H_{42}F_{21}O_6Eu$: C, 42.26; H, 3.55. Found: C, 42.19; H, 3.81.

A sample of Eu(hfbc)$_3$ was distilled in the same manner as Eu(facam)$_3$ but showed no change in the ir or nmr spectrum and performed no better as a chiral shift reagent.

Tris(3-trifluoroacetyl-*d*-camphorato)praseodymium(III), Pr(facam)$_3$. Following the standard procedure, to 2.98 g (1.20 mmol) of 3-trifluoroacetyl-*d*-camphor dissolved in 11.9 ml of 1 *N* sodium hydroxide was added 0.99 g (4.0 mmol) of praseodymium(III) chloride in 10 ml of ethanol. The reactants were stirred for 5 min, 20 ml of water was added, and the aqueous phase was decanted from the tan, resinous precipitate which formed.[27] The crude product was purified in the usual way to give 2.52 g (71% yield) of a light tan powder: mp indefinite (remains a solid up to 100°); ir ($CHCl_3$) identical with that for Eu(facam)$_3$; nmr (CCl_4) δ 0.96, 1.54, 4.30 (all resonances broad); uv max (hexane) 309 (ε 22,720), 270 mμ (weak shoulder); $[\alpha]^{20}D$ 222° (*c* 1.3, CCl_4).

Tris(3-heptafluorobutyryl-*d*-camphorato)praseodymium(III), Pr(hfbc)$_3$. Following the standard procedure, to 0.836 g (2.40 mmol) of 3-heptafluorobutyryl-*d*-camphor dissolved in 2.38 ml of 1 *N* sodium hydroxide was added 0.198 g (0.8 mmol) of praseodymium(III) chloride in 1 ml of 95% ethanol. After stirring for 5 min, 5 ml of water was added. The brown, resinous precipitate which formed was worked up in the usual manner to give 0.49 g (52% yield) of a light tan powder: mp indefinite (remains a solid up to 100°); ir ($CHCl_3$) identical with that for Eu(hfbc)$_3$; nmr (CCl_4) δ −5.34, 1.04, 3.66 (all resonances broad); uv max (hexane) 313 (ε 26,160), 270 mμ (weak shoulder); $[\alpha]^{20}D$ 176° (*c* 1.1, CCl_4).

Tris((*R*,*R*)-(−)-3,7-dimethyl-3,7-diphenyl-4,6-nonanedionato)europium(III). By the same method used to prepare the facam and hfbc europium chelates (except that europium(III) nitrate was used instead of the chloride) 0.88 g (2.6 mmol) of (*R*,*R*)-(−)-3,7-dimethyl 3,7-diphenyl-4,6-nonanedione was converted to 0.61 g (60% yield) of the europium chelate. The chelate was a viscous oil that failed to crystallize. The material was dried at room temperature under reduced pressure (<0.3 mm). The chelate had $[\alpha]^{25}D$ −35.6 (*c* 1.2, benzene); ir ($CHCl_3$) 1600 (broad and intense, C=O and C=C); nmr (CCl_4) δ −0.30, 0.83, 1.18, 5.70, 6.82 (all resonances broad). The europium chelate derived from *dl*-3,7-dimethyl-3,7-diphenyl-4,6-nonanedione was also a resinous oil. The optically active and racemic chelates had identical ir and nmr spectra.

Nmr Studies. In a typical experiment, the shift reagent was weighed into a nmr tube and dissolved in 0.3 ml of CCl_4. Substrate was measured into the tube with a syringe, the tube was capped, and the solution was mixed by tipping the tube back and forth. After recording a spectrum, more substrate was added and the process repeated.

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(25) An alternate preparation of this β-diketone ligand has recently been reported by B. Feibush, M. F. Richardson, R. E. Sievers, and C. S. Springer, Jr., *J. Amer. Chem. Soc.*, **94**, 6717 (1972).

(26) B. O. Linn and C. R. Hauser, *J. Amer. Chem. Soc.*, **78**, 6066 (1956).

(27) Longer reaction times caused the formation of crystalline material which melted sharply at 250° and gave an ir spectrum identical with the substance obtained from a short reaction time. The crystalline material, however, had such a low solubility in CCl_4 and $CDCl_3$ that it could not be used as a shift reagent.