a septum, stirring bar, and N_2 balloon was charged with 10 mL of dry tetrahydrofuran and 1.45 mL (0.002 32 mol) of *n*-butyllithium, 1.6 M, in hexanes. To this mixture was added 0.265 g (0.002 28 mol) of partially resolved (−)-(*R,R*)-*trans*-1,2-cyclohexanediol in 15 mL of dry tetrahydrofuran. (The diol had been obtained by chiral hydroboration–oxidation of 1-(trimethylsiloxy)cyclohexene.) After 30 min, iodomethane (0.15 mL, 0.002 41 mol) was added dropwise over 30 min. Then 5 mL of hexamethylphosphoric triamide was added in one portion. The mixture was stirred overnight and quenched by the addition of aqueous KOH. After 4 h, isolation by ether extraction and flash chromatography on silica gel gave 0.02 g (7%) of the title compound, needed for configurational assignment of the product of hydroboration of 1-methoxycyclohexene.

Registry No. **6a**, 931-57-7; **6b**, 29494-42-6; **6c**, 6651-36-1; **7a**, 1072-59-9; **7b**, 113548-17-7; **8b**, 113548-19-9; **8c**, 113548-20-2; **9a**, 113625-71-1; **9b**, 85761-38-2; **10a**, 113625-72-2; **10b**, 113625-73-3; **11b**, 113548-21-3; **11c**, 113548-22-4; **12**, 1072-86-2; (*S*)-**14**, 61229-00-3; (*R*)-**14**, 78843-64-8; **15** (dimer), 16997-72-1; $NH_4PO_4H_2$, 7722-76-1; $C_5H_{11}CO_2CH_2Ph$, 6938-45-0; $C_5H_{11}CO_2CHPh_2$, 113548-18-8; Ph_2CHOH, 91-01-0; $Cp_2TiCH_2(Cl)AlMe_2$, 67719-69-1; cyclohexanone dibenzyl ketal, 29494-49-3; cyclopentanone dibenzyl ketal, 2882-93-1; (+)-isopinocampheol, 24041-60-9.

Methodology for the Analysis of Products from Asymmetric Syntheses Using Chiral NMR Shift Reagents. Relative Complexation Constants of Enantiomers[1]

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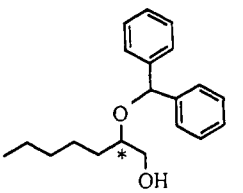
The enantiomeric excess (ee) of β-alkoxy alcohols and diols from asymmetric hydroboration of vinyl ethers was determined by 300-MHz NMR using chiral shift reagents. The use of Gaussian line narrowing and base-line correction to facilitate analyses is illustrated. Computer-assisted determination of the origins of shifted peaks with the aid of a calculated apparent complexation constant, *K*, is illustrated. The mathematics for simultaneous complexation of enantiomers having different *K* values is derived. For the first time, the contribution of differential complexation in NMR chiral shift studies was determined. For the case studied, both enantiomers were complexed to similar extents.

In the course of studies of the hydroboration–oxidation of vinyl ethers to give partially resolved β-alkoxy alcohols,[2] we became interested in the interpretation and optimal utilization of the NMR analyses obtained by using chiral Eu and Yb NMR shift reagents. In this paper we first illustrate some advantageous manipulations of the NMR data both at the console of the spectrometer or plotting station and by analysis using a personal computer. This portion of the paper deals with the application of known methodology and principles as they relate to modern instrumentation and to the needs of chemists involved in asymmetric synthesis.

We also report here the derivation of the mathematics required to separate the effects of differential complexation of enantiomers from the effects of differential shifting of NMR peaks in diastereomeric one-to-one complexes with NMR shift reagents. These separate effects were recognized, but not quantitatively evaluated, when chiral NMR shift reagents were first studied.[3] In a preliminary application of the derivation, we used a computerized, iterative procedure to determine the apparent *K* values for complexation of enantiomers obtained by asymmetric hydroboration of a vinyl ether. The term "apparent *K* values" refers here to equilibrium constants applicable to the widely employed one-to-one complex model.[4] Evidence for other types of complexes appears in the literature. However, all calculational efforts in the area may be regarded as simplified models when the full complexity of the systems is considered. For example, the possible existence of eight geometrical isomers has been discussed for one type of complex.[5]

Assessing Enantiomer Ratios. The spectra obtained from 14 additions of a solution of Yb(hfc)$_3$, tris[3-[(heptafluoropropyl)hydroxymethylene]-*d*-camphorato]ytterbium(III) derivative, to an NMR tube containing 2-(diphenylmethoxy)-1-heptanol (**11c**) (same numbering as in



11c

the accompanying paper) appeared to constitute an unusually favorable case for assessing the precision of analysis for enantiomer ratios. Examination of the spectra showed

(1) (a) Partial support by the National Institutes of Health, Grant 5-R01 AM31110-03, is acknowledged. (b) Partial support from the National Institutes of Health (Grant 1-S10-RR02425) and the National Science Foundation (Grant CHE-8411172) for purchase of the Bruker AM 300 NMR spectrometer is acknowledged. (c) Acknowledgment is made to Dr. James Knight, Physics Dept., USC, for the solution of simultaneous equations using computer algebra (SMP). (d) The advice of Dr. Ron Garber regarding processing of NMR spectra on the Aspect 1000 data station is acknowledged.

(2) Peterson, P. E.; Stepanian, M. S. *J. Org. Chem.*, preceding paper in this issue.

(3) Whitesides, G. M.; Lewis, D. W. *J. Am. Chem. Soc.* **1971**, *93*, 5914.

(4) *Nuclear Magnetic Shift Reagents*; Sievers, R. E., Ed.; Academic: New York, 1973.

(5) (a) Reference 3, p 58. (b) For a crystal structure, see: Horrocks, W. DeW.; Sipe, J. P., III; Luber, J. R. *J. Am. Chem. Soc.* **1971**, *93*, 5258.

0022-3263/88/1953-1907$01.50/0

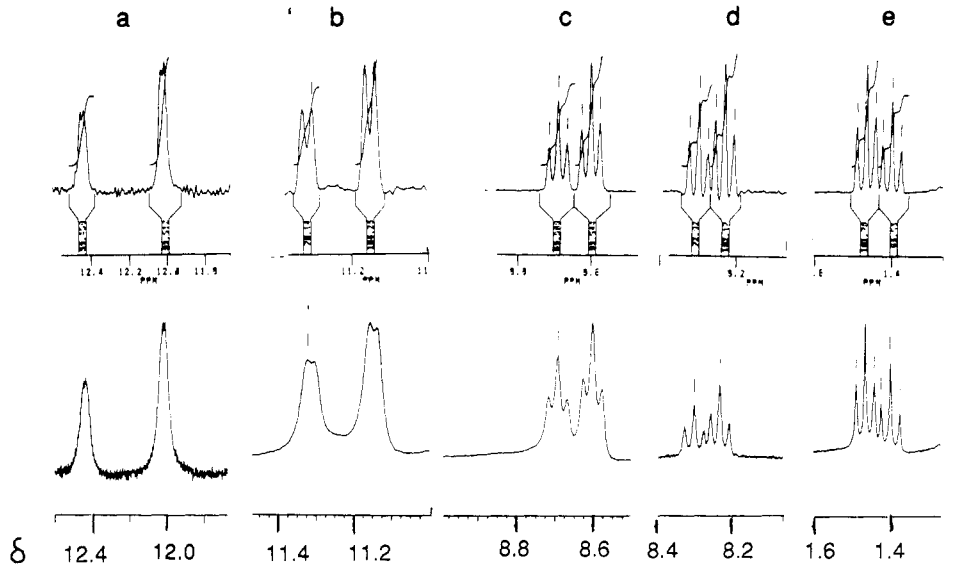


Figure 1. Original and reprocessed selected regions of the NMR spectrum of partially resolved 2-(diphenylmethoxy)-1-heptanol.

Table I. Enantiomer Ratios Determined from Five Regions of the NMR Spectrum of 2-(Diphenylmethoxy)-1-heptanol

	enantiomer ratio					
run,[a] μL of Yb	downfield ortho	upfield ortho	meta	para	methyl	av[b]
1, 100	1.508, 1.490[c]		1.402		1.392	1.434 ± 0.074
2, 100	1.547, 1.587[d]	1.493	1.430, 1.372[e]	1.400	1.525, 1.552	1.479 ± 0.079
2, 75	1.482, 1.727[c]	1.498 1.348[f]	1.445			1.475 ± 0.030

[a] Run 1, 2: 20-h and 1-h reaction time. [b] Plus or minus largest deviation. [c] Not narrowed. [d] Free induction pattern was reprocessed, with rechosen values of GB and LB. [e] Integration limits rechosen for same spectrum. [f] Deliberately overnarrowed (LB = −16 instead of −8).

five regions of promise for the analysis of enantiomers.

It is to be noted that the phenyl groups in one of the enantiomers of **11c** are nonequivalent because a chiral carbon atom is present. Accordingly, in the presence of a chiral shift reagent, spectra could exhibit a maximum of four peaks each for ortho, meta, and para hydrogens. In the case of the ortho hydrogens, all four peaks were observed in some of the spectra. This observation is illustrated in Figure 1, where the five useful regions of the spectrum are displayed, with peaks for ortho regions designated by the symbols a and b.

In the lower spectrum for each region, Figure 1, the shift-reagent-broadened peaks of the original spectrum (from exponential Fourier processing) are shown. In the accompanying upper spectrum, the effects of rephasing, base-line correction, and Gaussian line narrowing by as much as 16 Hz are shown. Also shown in Figure 1 are the meta hydrogen triplets of one of the phenyl groups of each enantiomer (c), the para hydrogen triplets of one phenyl group of each enantiomer (d), and the triplets of the chain-terminal methyl group of the enantiomers (e). Other phenyl hydrogens were not resolved. In Figure 2, the effect of line narrowing on a poorly separated peak used in the analysis of enantiomers of 1,2-hexanediol is shown.

It will be noted that line narrowing facilitated making a choice of regions for integration in many of the spectra. It is interesting that the obscured doublet structure of one of the downfield ortho hydrogens shown in Figure 1 (a) was revealed by line narrowing, making possible the assignment as an ortho peak. Accordingly, considerable information may be extracted by manipulation of shift-reagent-broadened spectra, if sufficient signal-to-noise ratio is available. It is necessary, however, to optimize the values of LB (the line-broadening parameter) and GB (the parameter that specifies the portion of the free induction decay that is transformed) to give the best results for each portion of the spectrum.[6]

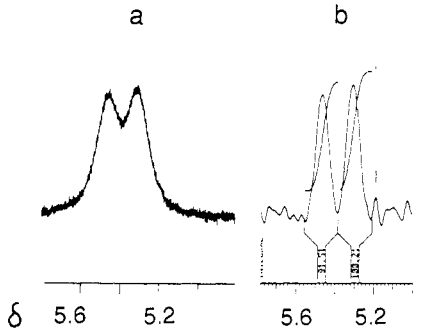


Figure 2. Original (a) and reprocessed (b) selected region of the NMR spectrum of partially resolved 1,2-heptanediol.

In Table I, ratios obtained from the spectral regions illustrated in Figure 1 are shown for the products of two hydroboration reactions (accompanying paper[2]) of 2-(diphenylmethoxy)-1-heptene, leading to partially resolved 2-(diphenylmethoxy)-1-heptanol. The enantiomeric excess values (ee) are given for reactions which were allowed to proceed for different times. Ratios measured for two amounts of shift reagent are given for run 2.

Deviations of ±5% from the average were observed among ratios for different regions of the spectrum. The averages of the ratios for two concentrations of shift reagent are fortuitously close, but should in general show better than ±5% precision if several peaks are available for integration. We have noted no systematic trends in the ratios. Increasing the number of pulses, here only 32,

(6) For a description of the early development of the line-narrowing method, see: (a) Clause, A. O. E.; Moody, D. C.; Rietz, R. R.; Rosenberry, T.; Schaeffer, R. *J. Am. Chem. Soc.* **1973**, *95*, 2496. In this paper only an approximation to the manipulation of the free induction decay by multiplication involving a Gaussian function was used. For a recent description of the method, now a standard utility, see: (b) Derome, A. E. *Modern NMR Techniques for Chemistry Research*; Pergamon: Elmsford, NY, 1987; p 25.

would be expected to increase the precision.

The results outlined above show that better determination of enantiomer ratios than might be expected from casual inspection of spectra may be made by appropriate processing of the spectra. Spectra of derivatives containing elements other than hydrogen (e.g., for ^{19}F in methoxy(trifluoromethyl)phenylacetic acid esters for alcohols)[7] may have advantages for some analyses of enantiomer ratios. However, hydrogen spectra shifted with chiral lanthanide reagents are often more readily available. The present work provides a guide to the precision that may be obtained when they are used in conjunction with spectral processing. In this connection, a recent paper reporting the effect of using CD_3CN or $(CD_3)_2SO$ to improve enantiomer analysis of polyols is of interest.[8]

Tracing Peaks to Their Origin and Finding Sensitivities to Shift Reagents by Using Computer-Determined Apparent Complexation Constants. In our study of hydroboration products,[2] curved plots of NMR chemical shifts versus the amount of shift reagent added were obtained for alkoxy alcohols shifted by the chiral Yb reagent. It was difficult to assign the origin of peaks that were obscured by overlap at the lower concentrations of shift reagent. We wondered whether a quantitative consideration of complex formation would be helpful. In many reported cases, the assumption of one-to-one complex formation (eq 1) serves as an adequate model to fit plots

$$MS = M + S \quad (1)$$

of experimental chemical shifts versus amount of shift reagent (or substrate) added.[4] Here MS represents the reagent–substrate (metal–substrate) complex, M is the shift reagent (metal), and S is the substrate.

The well-known solution of the quadratic equation for concentration as a function of the equilibrium constant for a reaction obeying eq 1 is

$$x = \tfrac{1}{2}\{S_0 + M_0 + K \pm [(S_0 + M_0 + K)^2 - 4(M_0S_0)]^{1/2}\} \quad (2)$$

where S_0 = moles/liter of substrate added, M_0 = moles/liter of metal shift reagent added, and x = moles/liter of complex, MS.

Precise studies in the literature have shown that slightly better fits may sometimes be obtained when both two-to-one and one-to-one (S to M) complexes are assumed to be present.[9] As noted earlier, all such assumptions may be regarded as models, since consideration of all species that may be hypothesized to be present appears to be beyond the reach of experimentation. We proceeded with the one-to-one model, since our goal was to rapidly achieve a reasonably accurate representation of the data.

A further stimulus for a quantitative investigation was the limited information in the literature concerning NMR shift studies of organic compounds using $CDCl_3$ solvent with Yb as the metal, and with the hfc ligand (our conditions). Accordingly, following the general approach of Shapiro and Johnston,[9] we wrote a BASIC-language program for the IBM personal computer to calculate, from eq 2, concentrations of complex MS for successive additions of shift reagent. The negative sign was used for the square root term, since the positive sign gave MS values larger than M_0. A plotting program previously written by P.E.P. was incorporated to allow the initial display of a plot of chemical shift versus amount of shift reagent. This display facilitated the correction of errors resulting from any incorrect transfer of data from the spectrometer printout to a data table used by the program.

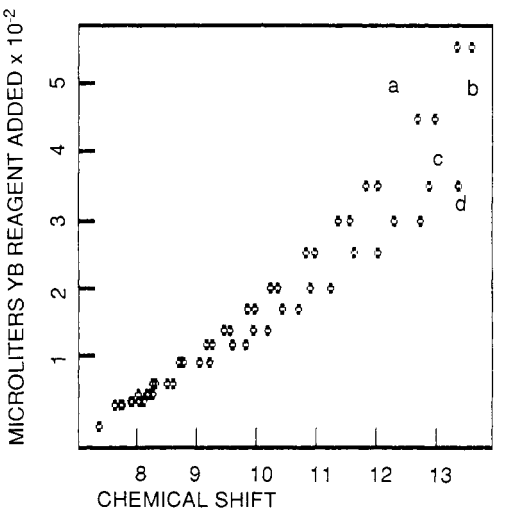


Figure 3. Plot of chemical shifts for 2-(diphenylmethoxy)-1-heptanol versus microliters of shift reagent solution added; upfield ortho hydrogens, a and b; downfield ortho hydrogens, c and d.

In the subsequent operation of the program, the best limiting shift (the chemical observed when the substrate is all complexed) for an arbitrarily chosen K value was then calculated from a sum based on all of the data points, by using an algebraic expression previously reported.[9] The sum of the squares for calculated minus observed shifts was then obtained, based on the limiting shift and the fractions of substrate complexed. Finally, K was automatically incremented and the calculation was repeated until the lowest least-squares sum was found. Best K values were obtainable in a few minutes, although the present version of the program depends on the operator to narrow the increment of K several times.

In the next step of the program, the chemical shifts were replotted versus the fraction complexed, to give a linearized plot. In Figures 3 and 4, the previously mentioned curved plot and the corresponding linearized plot are shown for some peaks of 2-(diphenylmethoxy)-1-heptanol (**11c**), whose analysis for enantiomers was described earlier in this paper. For each line of the linearized plot, a printout was obtained that listed the chemical shift at the origin (zero concentration of shift reagent), based on the least-squares slope and intercept. The program prompted the operator to specify the points to be used in the calculation of the slope. Tests showed that using only the later data points did, in fact, identify origins with useful accuracy. Accordingly, the goal of providing for computer-assisted tracing of points to their origin had been met.

Assessing the K Values for Two Enantiomers Present Simultaneously. Since the enantiomers present in the above-mentioned NMR shift experiment gave separate plots of peak position versus fraction complexed, it was of interest to see if analysis revealed different K values for dissociation of the diastereomeric complexes, MS. As has been mentioned, we have not found an example of such an assessment in the literature. In practice, K values obtained by the procedure described above were found to differ only slightly (by approximately 5%).

However, we realized that if the complexation constants were unequal, a more complex mathematical analysis would apply even for idealized one-to-one complexation. A tightly bound enantiomer would react preferentially with the first aliquots of shift reagent, leaving the other enantiomer relatively unaffected until the tightly bound en-

(7) Dale, J. A.; Dull, D. L.; Mosher, H. S. *J. Org. Chem.* **1969**, *34*, 2543.
(8) Sweeting, L. M.; Crans, D. C.; Whitesides, G. M. *J. Org. Chem.* **1987**, *52*, 2273.
(9) Shapiro, B. L.; Johnston, M. D., Jr. *J. Am. Chem. Soc.* **1972**, *94*, 8185.

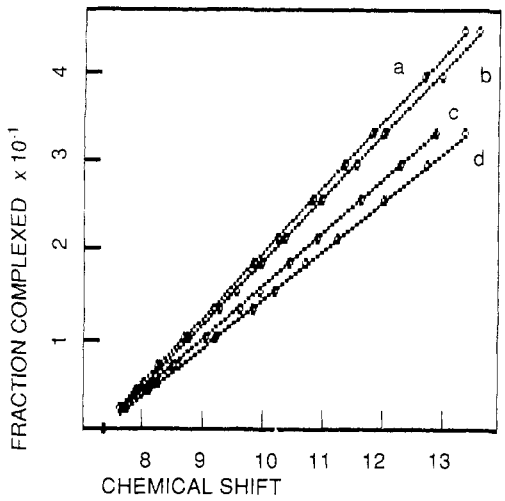


Figure 4. Plot of chemical shifts for 2-(diphenylmethoxy)-1-heptanol versus fraction of substrate complexed to shift reagent; upfield ortho hydrogens, a and b; downfield ortho hydrogens, c and d.

antiomer was removed by complexation. Although similar mathematics would apply for the simple case of titrating two acids having different pK values, we have not located an analysis for this case. Accordingly we derived the equations given below for competing substrates A and B (enantiomers in our case) reacting with lanthanide metal shift reagent M:

$$MA = M + A \quad (3)$$

$$MB = M + B \quad (4)$$

$$[(M_0 - x - y)(A_0 - x)]/x = K_a \quad (5)$$

$$[(M_0 - x - y)(B_0 - y)]/y = K_b \quad (6)$$

where x = moles/liter of metal complexed to A, y = moles/liter of metal complexed to B, M_0 = moles/liter of metal added, A_0 = moles/liter of A added, B_0 = moles/liter of B added.

Equation 6 may be solved for y as a function of x. Substituting $y(x)$ from eq 6 into eq 5 gave an expression containing x only. Several handwritten pages of terms were obtained containing powers of x through x^4. Fortunately for the accuracy of collecting these terms, we were able to have the equations solved by computerized algebra (see acknowledgement, footnote 1, this paper). The fourth-power terms cancelled, leaving the equation

$$[-K_a + K_b]x^3 + [K_a^2 + A_0K_a - 2A_0K_b - B_0K_a - K_aK_b + K_aM_0 - K_bM_0]x^2 + [A_0^2K_b + A_0B_0K_a + A_0K_aK_b - A_0K_aM_0 + 2A_0K_bM_0]x - A^2K_bM_0 = 0 \quad (7)$$

We incorporated this cubic equation into our program. The amount of complexed material MA was obtained as the root, x, of the cubic, for a trial value of K_a and K_b. In the program, the quadratic eq 2 was first used to get a trial value of MS. Multiplication of this value by the fraction of enantiomer A then gave a first trial value of x for use in solving the cubic eq 7 by the Newton–Rhapson method (successive approximation, based on slopes). The MA (x) value was stored and then used to obtain the first term of a sum,[9] from which the best limiting shift for the enantiomer A was obtained (for the initial K_a and K_b values). The cycle was repeated for each data point for A. The sum of the squares for the calculated minus the observed shifts for A was then obtained by using the calculated limiting shift and stored MA values.

The value y, the amount of MB, was then obtained for the first data point by one of two methods. In earlier work the cubic eq 7 was again employed, with an interchange of A_0 and B_0 and of K_a and K_b. However, there is a faster way to calculate MB after MA has been obtained by the iterative procedure. Algebraic manipulation yields eq 8 for MB. In later work the MB values from eq 8 were

$$MB = \{MA^2 - [MA(M_0 + A_0 + K_b)] + (M_0A_0)\}/(A_0 - MA) \quad (8)$$

stored after each MA value was obtained. Regardless of the method used, limiting shifts and sums of squares for calculated and observed shifts were obtained for enantiomer B, as described for A. Finally, the sums of the squares of the deviations for the A and B points were added to get a measure of the simultaneous fit of the calculated shifts to the observed data for both enantiomers.

The K_a and K_b values were automatically incremented separately to determine the values that gave the lowest sum of sums, described above. Approximately 1 min of computer time per K increment was used. Occasional manual adjustments of the magnitudes of K increments and of the initial K values resulted in obtaining the optimum K values to three significant figures after several hours of computation. Optimum pairs of K values were obtained for complexation of 2-(diphenylmethoxy)-1-heptanol enantiomers on the basis of the terminal methyl peaks, upfield ortho peaks and downfield ortho peaks, respectively.

The K values (equilibrium constants for dissociation of the complexes), their ratios, and the two differential limiting shifts (the change in the chemical shift upon complexation), calculated as described above, are given in Table II. As expected from earlier work with the quadratic solution (eq 2) to eq 1, K_a was found to be within a few percent of K_b. The magnitudes of differences were similar to the precision of the determination as judged from the values derived from separate peaks.

Caution should be exercised in assessing the data in Table II. Like all optimizations involving multiple parameters, broad minima may be present, leading to large error limits. In the present study there is a tradeoff between complexation constants and limiting shifts. As an example, a local minimum of the sum of sums, 0.032 95, occurs if K_b = 0.040 and K_a is varied until the minimum occurs at K_a = 0.0430, with limiting shifts 13.84 and 13.85. The overall lowest sum of sums, for K_b = 0.441 and K_a = 0.0462, is 0.028 39 with limiting shifts 14.16 (for A) and 14.35 (for B). In the first case, the more downfield chemical shift of B is reproduced by assigning it a lower dissociation constant. In the second case, part of the chemical shift difference between enantiomers arises from the difference in the limiting shifts. The difference in the dissociation constants is reduced. The latter fit is only 16% better for the sums of the squared differences in chemical shifts.

A second cautionary note is that the data column with the largest differences between calculated and observed values will tend to dominate the fitting process. K's for the other column may be adjusted more widely if the errors remain relatively small, compared to those for the first column.

A third cautionary note has to do with the loss of significant figures when numbers of comparable magnitudes are subtracted. Some insight may be offered by the following observations. When the K_a and K_b values are set to the same value, the cubic and quadratic equations are expected to be equivalent. Both K values were set to 0.044, and the fraction of substrate complexed was printed for each addition of shift reagent for each enantiomer, by using the quadratic and the cubic equation in its faster version,

Table II. Dissociation Constants and Limiting Differential NMR Shifts Evaluated from the Cubic Equation (7) for Simultaneous Complexation

group	K_a, major	K_b, minor	K ratio	dif lim shift, A	dif lim shift, B
CH_3	0.0568	0.0547	1.0384	2.405	2.080
upfield ortho	0.0462	0.0441	1.0476	14.348	14.159
downfield ortho	0.0453	0.0439	1.0763	18.495	17.355

which uses eq 8 for one enantiomer. All four lists differed only in the sixth or seventh number (e.g., 0.429 181 and 0.429 186). This result provides welcome confirmation that both the cubic and the quadratic portions of the program are correct.

Nevertheless, the sum of sums from the least-squares minimization varied substantially. Values for the minor enantiomer–quadratic, minor enantiomer–cubic and major enantiomer–quadratic, major enantiomer–cubic combinations were, respectively, 0.0169, 0.0249 and 0.0078, 0.0079. The respective limiting shifts differed by as much as 0.1 ppm (13.877, 13.864 and 14.532, 14.426). The lowest sum of sums from either the cubic or the quadratic method with K increments of magnitude 0.001 showed internal consistency, however, as illustrated by one set from the cubic equation, 0.0297, 0.0287, 0.0283, 0.0286, 0.0294.

Discussion

The first portion of our study provides an evaluation of the precision of determination of enantiomer ratios using high-field Fourier transform NMR with subsequent careful manual processing of the data for each region of the spectrum. Spectra that at first appearance showed limited promise proved to be quite usable. In addition to the example described in this paper, the enantiomer ratios of the accompanying paper[2] were obtained by the procedure described here.

The second portion of our study illustrates the value of straightening curved plots (of chemical shift versus amount of reagent added) by calculation of the fraction of substrate complexed, using the one-to-one complex model. Although known principles are used in this part of the study, the ability to evaluate K values within minutes from routinely acquired NMR data, and to display or print linear plots immediately by using a personal computer, makes the methodology of increased interest to synthetic chemists.

In addition to facilitating the location of the origins of shifted peaks, our program provides printed numerical values for the slopes of the straightened plots. These slopes represent the sensitivities of the various types of protons to shifting of their NMR spectra by the reagent.

That such sensitivities may be of use to synthetic chemists is shown by a recent study of Jerina et al.[10] in which the sensitivities, called gradients, were used in correlating the configuration of a series of epoxides. The gradients were obtained as described in the literature[11] from the initial straight-line portion of a plot of chemical shift versus molar ratio (reagent to substrate), for a relatively strongly complexed shift reagent.

Our procedure has the desirable feature of using all of the data points and requiring no recognition of points that constitute a linear initial region. The procedure applies when K values fall within a range that gives curved plots, described above. It will take more exploration to find which combinations of functional groups, shift reagents, and NMR solvents fall in this category. It is appropriate to note that more sophisticated applications of sensitivities (gradients), both absolute and relative, have been made by chemists interested in attempting to derive molecular geometries from these parameters.[12]

In the third part of our study, a new area was opened to investigation: the determination of the relative complexing ability of resolved chiral shift reagents toward enantiomers. In the first instance, examined here, minimal, if any, difference was found. If this observation proves to be generalizable, it raises the question of whether shift reagents can be designed that show substantial differential recognition of enantiomers. In any event, presently available shift reagents were effective in providing all of the enantiomer ratios needed in our study[2] of hydroboration of vinyl ethers.

Even if the one-to-one complex model proves not be the optimum model for our system, it seems likely that our conclusion that there was only marginally detectable differential complexing of enantiomers will remain valid. Regardless of the model, the plots for the separate enantiomers would exhibit different types of curvature if the K values were substantially dissimilar. It is unlikely that almost-equal K_a and K_b values would provide the best fits for any model in such circumstances. We note that the K values for the "two-to-one plus one-to-one" model have been related to those for the one-to-one model in some instances.[9]

Experimental Section

Analysis of 2-(Diphenylmethoxy)-1-heptanol for Enantiomeric Excess. The procedure is representative of analyses for other compounds. Equipment has been described in the accompanying paper.[2] To an oven-dried NMR tube was added 2-(diphenylmethoxy)-1-heptanol (0.0288 g, 0.0965 mmol) dissolved in 0.5 mL of $CDCl_3$. Successive additions of Yb(hfc)$_3$, tris[3-[(heptafluoropropyl)hydroxymethylene]-(+)-camphorato]ytterbium(III) reagent (0.14 M, dissolved in $CDCl_3$), were made, and spectra were determined by using the automated mode of the spectrometer. Amounts of reagent added may be discerned by examination of Figure 3. Spectra judged to be suitable for ee determination were transferred to the Aspect 1000 plotting station and processed as described earlier in this paper. For the larger concentrations of shift reagent, the most rapidly shifting peaks (from CHOH or CHOR) were off scale downfield at the standard chemical shift range (−1 to 19 ppm) and were not examined. These peaks, broadened by coupling, also were not promising for ee determination for the smaller concentrations of shift reagent. Their signal-to-noise ratio was low in the more shifted spectra.

Analysis of 1,2-Cyclohexanediol. This analysis is described because the crossing of peaks as shift reagent was added made many spectra uninterpretable until peak tracing was used. The spectrum with no shift reagent added showed peaks whose structural origin we have not determined at 3.320 (br, 2 H), 2.81 (br, 2 H, OH?), 1.94 (br, 2 H), 1.67 (br, 2 H), and 1.23 (br, 4 H). This and other diols showed linear plots of chemical shift versus the amount of shift reagent added, presumably owing to strong complexation. Two pairs of peaks were suited for analysis at several of the higher concentrations of shift reagent. Tracing the pairs to their origin by use of our plot program showed that the downfield pair, which consisted of broadened triplets after line narrowing, was the faster shifting pair which had its origin at the more upfield position, 1.23. The upfield pair, a broadened doublet, originated at the more downfield position, 1.67. A printout of expected peak positions at lower concentrations of shift reagent allowed the overlapping peaks to be identified.

Registry No. **11c**, 113628-00-5; **4b**(hfc)$_3$, 80464-74-0.

(10) Yeh, H. J.; Balani, S. K.; Yagi, H.; Greene, R. M. E.; Sharma, N. D.; Boyd, D. R.; Jerina, D. M. *J. Org. Chem.* **1986**, *51*, 5439.

(11) Sanders, J. K. M.; Hansen, S. W.; Williams, D. H. *J. Am. Chem. Soc.* **1972**, *94*, 5325.

(12) (a) Reference 4, p 129. (b) For leading references, see: Raber, D. J.; Peters, J. A.; Nieuwenhuizen, M. S. *J. Chem. Soc., Perkin Trans. 2* **1986**, 853.