a homonuclear tetrahedral metal cluster, these would constitute degenerate paths. Finally, just as with the conventional base adducts of BH_3, the reactions of I with Lewis bases are a sensitive function of reaction parameters.

Acknowledgment. The support of the National Science Foundation (CHE-84-08251) is gratefully acknowledged.

Registry No. [I]PPN, 102233-76-1; [II]PPN, 102233-78-3; [III]PPN, 102233-85-2; [IV]PPN, 102339-50-4; $[Fe_3(CO)_8(\mu\text{-}CO)(PhMe_2P)BH_2]$PPN, 102233-80-7; $(\mu\text{-}H)Fe_3(CO)_9(\mu\text{-}CO)BH(CH_3)$, 102233-81-8; $[Fe_3(CO)_8(\mu\text{-}CO)(PhMe_2P)BH(CH_3)]$PPN, 102233-84-1; H_2O, 7732-18-5; NEt_3, 121-44-8; $PhMe_2P$, 672-66-2; CO, 630-08-0; $[HFe_3(CO)_{11}]^-$, 55188-22-2; $PhMe_2{\cdot}BH_3$, 35512-87-9; $Fe(CO)_3(PhMe_2P)_2$, 52253-91-5; $[(\mu\text{-}H)Fe_3(CO)_8(\mu\text{-}CO)(PhMe_2P)_2]$PPN, 102233-87-4; Fe, 7439-89-6.

Enantiomeric Purity Determination of 1,2-Diols through NMR Spectroscopy without Chiral Auxiliaries[1]

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Abstract: The use of optically active chiral auxiliaries for enantiomeric purity determinations by NMR can be avoided if the appropriate conditions for the "self-discrimination" of enantiomers are met. Molecular aggregation under fast-exchange conditions is shown to potentially render self-discriminating chiral molecules in nonracemic mixtures through the generation of diastereomeric relationships among groups. This phenomenon should not a priori be considered exceptional. The general principles of self-discrimination are analyzed in detail and conveniently applied in the case of dioxastannolanes, which are known to be strongly associated in solution. 1,2-Propanediol (**1**) and 1-phenyl-1,2-ethanediol (**2**) have been chosen as representative examples of the class of 1,2-diols, and are converted to the corresponding 2,2-dibutyl-1,3,2-dioxastannolanes (**3** and **4**) by means of achiral dibutyltin reagents. Mixtures of various enantiomeric excess of **3** and **4**, respectively, have been studied by ^{13}C NMR spectroscopy in concentrated solutions in $CDCl_3$, where they show the phenomenon of self-discrimination. The fractional intensities of the signals from the *R* and *S* enantiomers can be used for measurements of enantiomeric excess with an estimated accuracy of ±2%.

The determination of enantiomeric purity of chiral compounds is usually accomplished by exploiting their interaction with a different, optically active species. Based on this principle, many methods and techniques have been developed:[2,3] for instance, in NMR, excellent results are often achieved by using chiral solvents or auxiliaries to resolve signals from the two enantiomers in diastereomeric adducts.[2,3f-i]

When stable compounds are formed, or the parent enantiomeric species exchange slowly among the adducts, each diastereomeric adduct gives rise to a different NMR spectrum; when the exchange is fast, each parent enantiomer gives rise to a different spectrum, because the enantiomers spend at least fractions of time in diastereotopic environments. In the latter case adduct formation need not be complete nor the complexing agent (chiral auxiliary) need be enantiomerically pure.

Chiral auxiliaries are not an absolute requirement. It has been recently shown[4,5] that, when a compound, present as two enantiomers, *d* and *l*, forms kinetically inert dimers, the difference between the *dd* (*ll*) and *dl* (*ld*) diastereoisomers is detectable by NMR. Here the applicability of the method depends on the knowledge of the relative tendency to form homo- or heterodimeric aggregates.

The next logical step in the exploitation of achiral reagents for enantiomeric purity determinations would be to induce the formation of dimers, among which the interchange of monomeric units can be fast on the NMR time scale. As long as the enantiomeric composition differs from that of the racemic mixture, different signals from the *d* and *l* units are expected, with intensities directly proportional to [*d*] and [*l*]. The mixture would thus exhibit self-discrimination.

Although a few examples of self-discrimination under fast-exchange conditions have appeared in the literature,[6] this phenomenon is still considered exceptional.[2d] The purpose of the present paper is to investigate the potentiality of this phenomenon and to provide criteria for its general application. We show that self-discrimination can be conveniently used for the enantiomeric purity determination of chiral 1,2-diols, whose difficulty has been already pointed out.[3f] Diols are easily converted into dioxastan-

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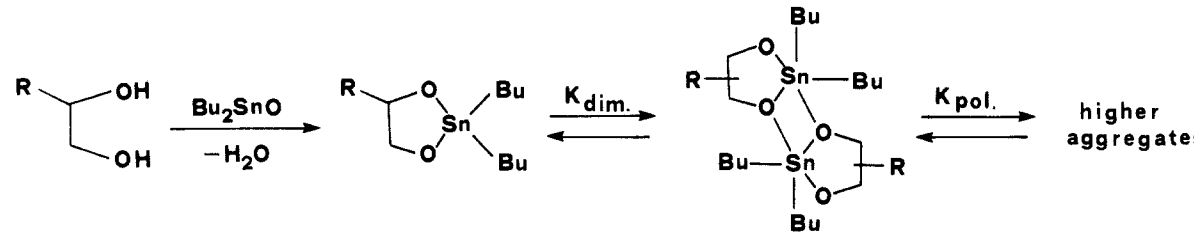
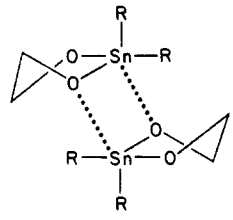
Scheme I



nolanes by achiral (commercial) dialkyltin(IV) reagents;[7] dioxastannolanes are known[7] to form aggregates of the type below in solution in apolar solvents. The amount of monomeric species



in concentrated solutions at room temperature has been found to be negligible;[1,8] although the monomer–dimer equilibria are slow on the NMR time scale, fast exchange of monomeric units among dimers occurs through the formation of small amounts of higher aggregates. Two representative examples of chiral diols have been chosen for investigation by ^{13}C NMR spectroscopy, which appeared to be the appropriate technique in this case. ^{1}H NMR spectra of diols of this type have been shown to be too complex for the present purpose.[3f,g]

Experimental Section

Materials. Racemic (Fluka >98%; bp 83–85 °C/11 mmHg) and enantiomerically pure [(*S*)-(+), Aldrich, 99%; bp 186–188 °C/765 mmHg] 1,2-propanediol, racemic (Aldrich, 97%; mp 66–68 °C) and enantiomerically pure [(*S*)-(+), Fluka, >98%; mp 66–68 °C] 1-phenyl-1,2-ethanediol, dibutyltin oxide (Fluka, purum, mp >300 °C), and deuteriochloroform (Merck, 99.5%) were used without further purification. Racemic (r.c.) and enantiomerically pure (*S*) (e.p.c.) 4-phenyl- and 4-methyl-2,2-dibutyl-1,3,2-dioxastannolanes were prepared, according to known procedures,[7] by azeotropic dehydration of the corresponding diols in toluene in the presence of dibutyltin oxide; yields were essentially quantitative. Products were recrystallized from benzene and traces of dibutyltin oxide were removed by centrifugation of a concentrated chloroform solution of dioxastannolanes. Products gave correct analyses for the expected compounds and showed physical and spectroscopical properties in agreement with literature data (all melting points were uncorrected; δ values in parts per million (ppm) from Me_4Si, using $CDCl_3$ as the internal secondary reference at 76.90 ppm; 0.85 M solutions; 33 °C; average $^{n}J[^{117/119}Sn-^{13}C]$ coupling constants are given).

4-Methyl-2,2-dibutyl-1,3,2-dioxastannolane, r.c. (3a): white microcrystalline powder; mp 191–192.5 °C [lit.[9] mp 185–188 °C]; ^{13}C NMR $CHCH_3$, 20.65 (^3J = 22 Hz); *C*HMe, 68.11; CH_2CHMe, 69.11; $(CH_2)_\alpha$, 22.77 (^1J = 634 Hz); $(CH_2)_\beta$, 27.35, 27.24 (^2J = 35 Hz); $(CH_2)_\gamma$, 26.76, 26.69 (^3J = 104 Hz); $(CH_3)_\delta$, 13.33 (^4J = 6 Hz). Anal. ($C_{11}H_{24}O_2Sn$) C, H.

4-Methyl-2,2-dibutyl-1,3,2-dioxastannolane (*S*), e.p.c. (3b): white microcrystalline powder; mp 191–193 °C; ^{13}C NMR $CHCH_3$, 20.68 (^3J = 22 Hz); *C*HMe, 68.04; CH_2CHMe, 69.10; $(CH_2)_\alpha$, 22.75, 22.64 (^1J = 634 Hz); $(CH_2)_\beta$, 27.35, 27.26 (^2J = 35 Hz); $(CH_2)_\gamma$, 26.76, 26.70 (^3J = 104 Hz); $(CH_3)_\delta$, 13.34 (^4J = 6 Hz). Anal. ($C_{11}H_{24}O_2Sn$) C, H.

4-Phenyl-2,2-dibutyl-1,3,2-dioxastannolane, r.c. (4a): white microcrystalline powder; mp 191–193 °C [lit.[10] mp 186–188 °C]; ^{13}C NMR Ph, C_{ipso} 143.24 (^3J = 24 Hz); $C_{o,m}$ 127.99, 126.57; C_p 127.33; *C*HPh, 75.70; CH_2CHPh, 68.98; $(CH_2)_\alpha$, 22.56 (^1J = 615 Hz); $(CH_2)_\beta$, 27.24 (^2J = 33 Hz); $(CH_2)_\gamma$, 26.76, 26.64 (^3J = 102 Hz); $(CH_3)_\delta$, 13.40 (^4J = 5 Hz). Anal. ($C_{16}H_{26}O_2Sn$) C, H.

4-Phenyl-2,2-dibutyl-1,3,2-dioxastannolane (*S*), e.p.c. (4b): white microcrystalline powder; mp 192–194 °C; ^{13}C NMR Ph, C_{ipso} 143.15 (^3J = 24 Hz); $C_{o,m}$ 127.99, 126.58; C_p 127.35; *C*HPh, 75.64; CH_2CHPh, 69.11; $(CH_2)_\alpha$, 22.63, 22.31 (^1J = 617 Hz); $(CH_2)_\beta$, 27.23 (^2J = 32 Hz); $(CH_2)_\gamma$, 26.72, 26.65 (^3J = 101 Hz); $(CH_3)_\delta$, 13.38 (^4J = 5 Hz). Anal. ($C_{16}H_{26}O_2Sn$) C, H.

Instruments and Techniques. Proton-decoupled ^{13}C NMR spectra were recorded at 20.00 MHz on a Varian FT80 A instrument, equipped with a variable-temperature appratus, and at 75.46 MHz on a Bruker CXP 300 instrument. Precise chemical shift values were obtained using high digital accuracy, and the maximum estimated error was ±0.003 ppm on δ values and ±0.0015 on $\Delta\delta$ values. Unequivocal assignment of signals was performed using $J[^{13}C-^{117/119}Sn]$ coupling constants and SEFT[11] pulse sequences. Spectral simulation and graphic plotting of equations were performed on a HP 86B desk computer.

Results

Starting from racemic (r.c.) (**a**) and enantiomerically pure (e.p.c.) (**b**) compounds, 1,2-propanediol (**1**) and 1-phenyl-1,2-ethanediol (**2**) were quantitatively converted to 2,2-dibutyl-1,3,2-dioxastannolanes (**3** and **4**) (Scheme I). The proton decoupled ^{13}C NMR spectra at 33 °C of concentrated (0.85 M) deuteriochloroform solutions of compounds **3a** and **4a** are different from those of **3b** and **4b**, respectively (see experimental section). Complex exchange processes are evident from variable-temperature studies and will be discussed elsewhere.[12] It has been observed, in line with previous findings,[1,8] that fast scrambling of monomeric units among aggregates occurs at room temperature.

Different shifts for **3a** and **4a** with respect to **3b** and **4b** are due to the presence of dimeric species **5** and **6** in which strong diastereomeric interactions occur. Chemical shift differences were particularly evident for the asymmetric carbon atom of compounds **3** and for the ipso carbon atom of the phenyl group of compounds **4**. Mixtures of **3** of enantiomeric excess (ee) varying between 0% and 100% were thus prepared by mixing 0.85 M solutions of **3a** and **3b** in $CDCl_3$ and monitored at 20 MHz and 33 °C. Analogous experiments were performed on compounds **4**. The resulting chemical shifts are reported in Tables I and II. Apart from the r.c. and the e.p.c., which showed a single line each, every mixture of different ee gave a pair of signals; with increasing ee, one signal moves downfield, decreases in intensity, and disappears for ee equal

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Table I. ^{13}C NMR Parameters for the Asymmetric Carbon in Mixtures of **3a** and **3b**[a]

R/S[b] (ee)	δ_R[c,d]	δ_S[c]	$\Delta\delta$[e]	I_R/I_S[f]	ee[g]
50.0/50.0 (0.0)	68.114	68.114			
39.9/60.1 (20.2)	68.126	68.096	0.030	40/60	20 (0)
30.0/70.0 (40.0)	68.146	68.084	0.062	30/70	40 (0)
25.0/75.0 (50.0)	68.158	68.079	0.079	24/76	52 (+2)
20.1/79.9 (59.8)	68.154	68.062	0.092	19/81	62 (+2)
10.0/90.0 (80.0)	68.174	68.052	0.122	9/91	82 (+2)
5.6/94.4 (88.8)	68.179	68.038	0.141	6/94	88 (−1)
0/100 (100)		68.038			

[a] Proton decoupled spectra recorded at 20 MHz, 33 °C, 0.85 M total concentration in $CDCl_3$. [b] Effective enantiomeric ratio. [c] Chemical shift values (ppm) from Me_4Si measured using $CDCl_3$ as the internal secondary reference at 76.900 ppm. Values are averaged over at least two independent runs. The estimated error is ±0.003 ppm. The line widths range between 0.8 and 1.4 Hz for compound **3** and between 0.7 and 1.0 Hz for compound **4**. [d] Chemical shift values have been obtained from spectral simulation when necessary. [e] The estimated error on chemical shift differences is ±0.0015 ppm. [f] Measured by matching with simulated spectra for compound **3** and by direct integration for compound **4**. [g] Deviations from effective values in parentheses. [h] Not measurable.

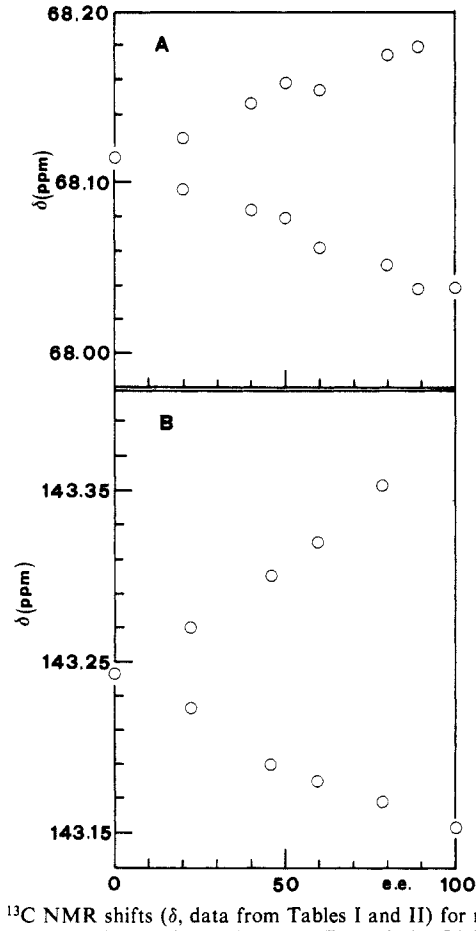

Figure 1. ^{13}C NMR shifts (δ, data from Tables I and II) for mixtures of **3a** and **3b** (A) and **4a** and **4b** (B) vs. ee. For (A) the C* has been monitored, for (B) the C_{ipso} of the phenyl group.

to 100%; the other signal moves upfield, increases in intensity, and approaches the position of the e.p.c. signal. This behavior is illustrated in Figure 1. The differences in chemical shift are plotted as a function of ee in Figure 2; the data appear to be related to the ee for both compounds.

A second feature clearly appears from the data in Tables I and II: the intensities of the pairs of signals closely reflect the relative amounts of the *R* and *S* enantiomers in the mixtures. This behavior is shown in Figure 3.

The same results are obtained when dibutyltin oxide is reacted with a mixture of *R* and *S* diols of known ee. The integrated intensities of the two signals always agree, within 2%, with the

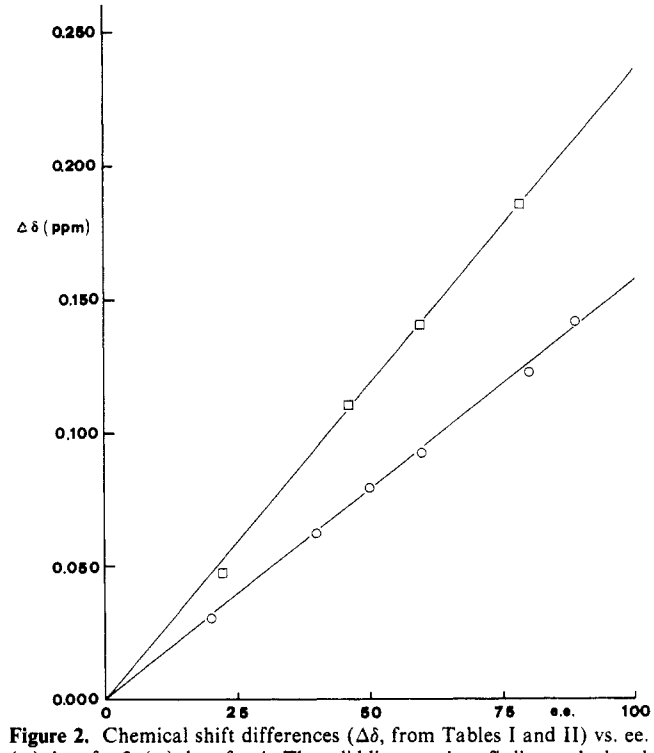

Figure 2. Chemical shift differences ($\Delta\delta$, from Tables I and II) vs. ee. (○) data for **3**; (□) data for **4**. The solid lines are best fit lines calculated from (A22).

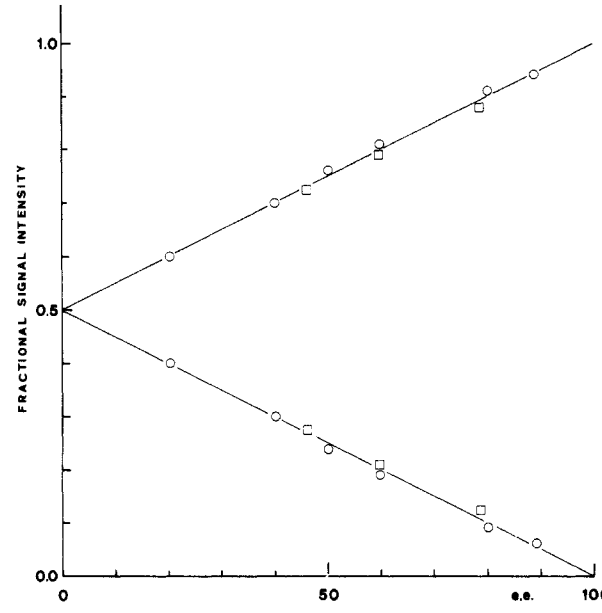

Figure 3. Fractional signal intensities (Tables I and II) vs. ee. (○) data for **3** calculated by spectral simulation; (□) data for **4** measured by direct integration. The solid line is calculated from (1).

calculated amounts of *R* and *S* forms.

Moreover, when a sample of **4** of ee 56.3% was allowed to react with the stoichiometric amount of dibutyltin chloride in $CDCl_3$ by stirring the mixture at room temperature for 1 h over anhydrous sodium carbonate, the ^{13}C NMR spectrum of the filtered mixture showed an ee of 56%, in excellent agreement with the known value.

The concentration dependence of the chemical shifts has been investigated for compounds **3** (Table III). Chemical shift differences are only slightly dependent on concentration, in contrast to the chemical shift values themselves which exhibit a strong dependence on the latter. The sensitivity to concentration is likely to be the cause of the scatter of the chemical shift values shown in Figure 1. Temperature also affects both the chemical shifts and their differences: for an *R*/*S* ratio of 20/80 (compounds **4**) the chemical shift difference decreases from 0.140 to 0.114 ppm

Table II. ^{13}C NMR Parameters for the C_{ipso} Carbon in Mixtures of **4a** and **4b**[a]

R/S[b] (ee)	δ_R[c,d]	δ_S[c]	$\Delta\delta$[e]	I_R/I_S[f]	ee[g]
50.0/50.0 (0.0)	143.243	143.243			
38.9/61.1 (22.2)	143.270	143.223	0.047	*h*	*h*
27.0/73.0 (46.0)	143.300	143.190	0.110	27/73	46 (0)
20.2/79.8 (59.6)	143.320	143.180	0.140	21/79	58 (−2)
10.8/89.2 (78.4)	143.353	143.168	0.185	12/88	76 (−2)
0/100 (100)		143.153			

[a] Proton decoupled spectra recorded at 20 MHz, 33 °C, 0.85 M total concentration in $CDCl_3$. [b] Effective enantiomeric ratio. [c] Chemical shift values (ppm) from Me_4Si measured using $CDCl_3$ as the internal secondary reference at 76.900 ppm. Values are averaged over at least two independent runs. The estimated error is ±0.003 ppm. The line widths range between 0.8 and 1.4 Hz for compound **3** and between 0.7 and 1.0 Hz for compound **4**. [d] Chemical shift values have been obtained from spectral simulation when necessary. [e] The estimated error on chemical shift differences is ±0.0015 ppm. [f] Measured by matching with simulated spectra for compound **3** and by direct integration for compound **4**. [g] Deviations from effective values in parentheses. [h] Not measurable.

Table III. Effect of Concentration on *C Chemical Shifts of **3** for a Mixture of 59.8% ee[a]

concn, M	δ_R	δ_S	$\Delta\delta$
0.85	68.154	68.062	0.092
0.42	68.275	68.184	0.091
0.21	68.331	68.242	0.089

[a] Data obtained at 75.46 MHz using $CDCl_3$ central line as an internal secondary reference at 76.900 ppm from Me_4Si. Estimated accuracy of 0.001 ppm.

when the temperature increases from 33 to 59 °C, without appreciable variation in line width.

In contrast, intensity ratios were completely insensitive to concentration or temperature variations in the above ranges.

Discussion

A complete treatment of the phenomenon of self-discrimination of the enantiomeric species is given in Appendix section I. The salient result is that, regardless of the nature and chemical composition of the aggregates, two NMR signals are always expected from each nucleus in the two enantiomers, with intensities I directly proportional to the concentrations of R and S (C_R and C_S) as long as fast exchange occurs among all the dominant species in solution (eq 1). This concept implies that dimer formation, if rapid on

$$\frac{I_R}{I_S} = \frac{C_R}{C_S} \tag{1}$$

the NMR time scale, need not be complete or, as in the present case, that dissociation into monomers may even be slow if the latter are present in negligible amounts.

Comparison of experimental with calculated data for the fractional signal intensities (Figure 3), together with the observed insensitivity of I_R/I_S ratios to increase in temperature, shows unequivocally that fast scrambling of monomeric units is occurring. For both cases (**3** and **4**) the agreement is excellent, proving that integration of signals can be used as a *direct* measure of the ee: a single measure provides an immediate estimate of the C_R/C_S ratio. The latter is independent of such parameters as temperature, concentration, and hetero/homodimer ratio (see Appendix section II), as long as fast-exchange conditions are met.

Depending on the intrinsic sensitivity of the system to discrimination, integration of signals might not be straightforward, but simple matching with computer-simulated signals gives excellent estimates of the intensities. Thus, for compound **3**, deviations of 1–2% could be easily detected, giving an estimated precision of ±2% on ee values. Spectral simulation was not necessary for compound **4**: the reported data were in fact obtained by direct integration of the signals, affording the same estimated precision as above. Therefore, formation of dioxastannolane dimers turns out to be a simple and accurate way for the ee determination of 1,2-diols through NMR, and in general, the formation of kinetically labile dimers should be considered as a promising tool for ee determinations.

Further Considerations. Focusing on those cases where dimers are the dominant species, the treatment developed in Appendix section II can be used to (1) obtain information on the hetero/homodimer distribution in the present systems from the analysis

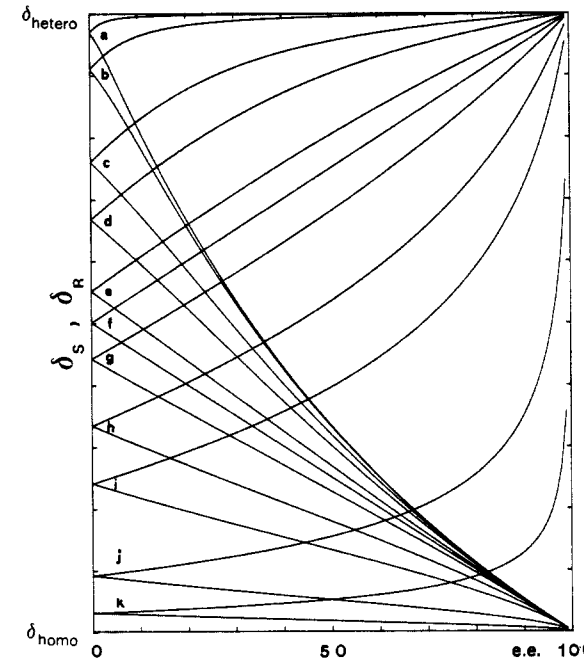

Figure 4. Calculated chemical shifts vs. ee for nuclei in the R and S enantiomers at various exemplificative K values according to (A16) and (A17). K values are (a) 4000, (b) 400, (c) 40, (d) 16, (e) 6, (f) 4 (eq A20 and A21), (g) 2.5, (h) 1, (i) 0.4, (j) 0.04, and (k) 0.004.

of the chemical shifts and (2) establish criteria to predict whether a system should exhibit self-discrimination.

The relative amounts of hetero- and homodimers can be expressed as eq 2. Equations A16–A18 and A20–A22 in Appendix section II show the chemical shifts of the R and S signals, δ, and

$$K = \frac{[RS]^2}{[RR][SS]} \tag{2}$$

their separation, $\Delta\delta$, for $K \neq 4$ and $K = 4$,[13] respectively. δ and $\Delta\delta$ values calculated according to the above equations are also shown in Figures 4 and 5, respectively, as a function of ee at various K values. It may be noted that both δ and $\Delta\delta$ are linear functions of ee *only* for $K = 4$. When K tends to zero, $[RS]$ tends to zero, $[RR]$ tends to $C_R/2$, and δ_R and δ_S tend to δ_{homo}, independently of the enantiomer excess. This implies that *a system unable to form heterodimers does not give rise to self-discrimination.* When K tends to infinity in excess of S, $[RS]$ tends to C_R and $[RR]$ tends to zero. Under such conditions the maximum self-discrimination for a given ee is exhibited, i.e., eq 3. Such

$$\Delta\delta = \frac{1}{f_S}(\delta_{hetero} - \delta_{homo})ee/100 \tag{3}$$

(13) This case requires special consideration: when homo- and heterodimeric species have equal enthalpy, K is equal to 4 on account of entropic factors that favor the formation of the mixed species. K is expected to be close to 4 whenever steric interactions between monomeric moieties are similar in both the RS and RR (SS) dimers.

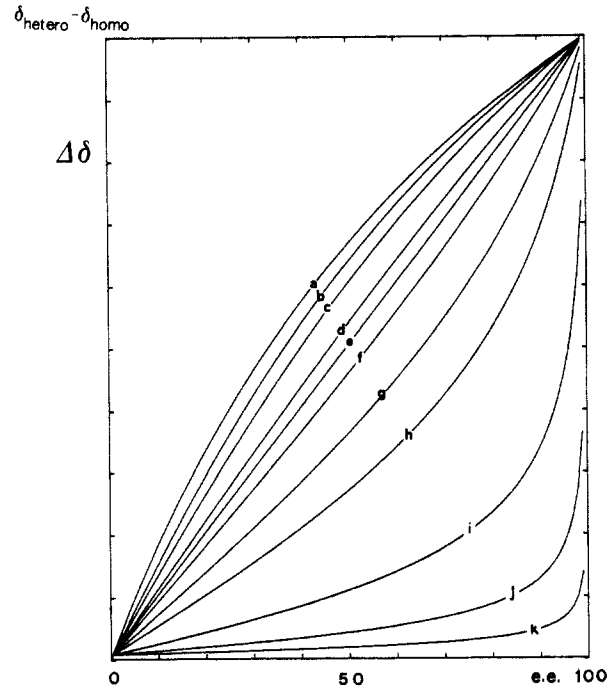

Figure 5. Calculated $\Delta\delta$ values vs. ee at various K values according to (A18). K values are (a) 40 000 ($\simeq\infty$), (b) 40, (c) 16, (d) 6, (e) 4 (eq A22), (f) 2.5, (g) 1, (h) 0.4, (i) 0.04, (j) 0.004, and (k) 0.0004.

chemical shift difference is larger than that for $K = 4$ by a factor $1/f_S$. Therefore, *the maximum self-discrimination is exhibited when heterodimers are favored.*

Comparison between experimental and calculated δ values for the present dioxastannolanes (Figures 1 and 4) shows that the K value is equal or close to 4 within experimental error for both the methyl- and the phenyl-substituted derivatives. This demonstrates no strong preference in the diastereomeric aggregation and comparable population of homo- and heterodimers in a racemic mixture. Even more striking is the correlation between experimental and calculated $\Delta\delta$ values (Figures 2 and 5): the excellent linearity with ee confirms the estimate of $K = 4$ for both series; their slopes give an indication of the sensitivity of the specific system to self-discrimination, and direct extrapolation provides $\delta_{hetero} - \delta_{homo}$ values of 0.157 and 0.236 ppm for **3** and **4**, respectively. These values show the size of the effect to be expected for systems of this kind.

Finally, it should be noted that, for $K = 4$, the correlation plot of $\Delta\delta$ also provides a very accurate measure of ee; however, although $\Delta\delta$ in quite insensitive to concentration, extrapolated values for $\delta_{hetero} - \delta_{homo}$ are required, which obviously cannot be obtained from a single measurement. Furthermore, attention must be paid to the possibility that the system might have $K \neq 4$, in which case $\delta_{hetero} - \delta_{homo}$ cannot be obtained by direct extrapolation.

Conclusions

The present work shows that conversion to dioxastannolanes by means of achiral tin reagents is a simple method for the enantiomeric purity determination of chiral diols. The derivatization of diols is easy and quantitative and no special care is required in handling the products. ^{13}C NMR spectra of concentrated solutions in $CDCl_3$ show splitting of some signals whose intensities are used to accurately measure the ee. Matching with simulated spectra or direct intensity evaluations for several mixtures of different ee provides values with an estimated error of $\pm 2\%$. The reported examples are shown to fit a general treatment for the principle of self-discrimination under fast-exchange conditions; a detailed analysis of the basic aspects of this method has been given. The use of inexpensive reagents and the simplicity of the procedure and its accuracy, comparable to that of other NMR methods, are among the advantageous features of the present technique, whose extension to other classes of compounds is under current investigation.

It should be emphasized that this method is potentially of general validity, since (1) many organic molecules are known to undergo association under appropriate conditions[14] or can be forced to form molecular aggregates by the use of specific reagents, (2) intensities of NMR signals can be measured with reasonable accuracy even with routine instruments such as the the one employed in the present research, and (3) no a priori knowledge of any physicochemical property of the pure enantiomers is required.

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Appendix

I. General Treatment. The phenomenon of self-discrimination of the enantiomeric species may be described in general terms. Consider a solution constituted by a mixture of enantiomeric molecules l and d, in analytical concentrations C_l, and C_d; their mole fractions are expressed as

$$f_l = \frac{C_l}{C_l + C_d} \qquad f_d = \frac{C_d}{C_l + C_d} \tag{A1}$$

The ee for the mixture is then defined as

$$ee/100 = \frac{C_l - C_d}{C_l + C_d} = f_l - f_d \tag{A2}$$

Allow now for the possibility of the formation of aggregates of any stoichiometry, up to $n$mers. Then, in general,

$$C_l = \sum_{i=1}^{n}\sum_{j=0}^{n-i} i[l_i d_j]$$

$$C_d = \sum_{i=1}^{n}\sum_{j=0}^{n-i} i[d_i l_j] \tag{A3}$$

where $l_i d_j$ is a generic aggregate of i molecules of l and j molecules of d, with i and j being any integer as long as their sum does not exceed n. If all of the above species are in fast exchange, the chemical shift of a given nucleus in the l enantiomers, δ_l, can be written as

$$\delta_l = \sum_{i=1}^{n}\sum_{j=0}^{n-i} i\frac{[l_i d_j]}{C_l}\delta_{l(l_i d_j)} \tag{A4}$$

where $\delta_{l(l_i d_j)}$ denotes the chemical shift of the nucleus in the l molecules of the $l_i d_j$ aggregate. Likewise,

$$\delta_d = \sum_{i=1}^{n}\sum_{j=0}^{n-i} i\frac{[d_i l_j]}{C_d}\delta_{d(d_i l_j)} \tag{A5}$$

As long as fast-exchange conditions hold, eq A4 and A5 are general, since they do not contain any assumption regarding the number, type, distribution, and geometry of the aggregates. It is immediately noted that $d_i l_j$ and $l_i d_j$ are either an enantiomeric pair or a meso compound; therefore, $\delta_{l(l_i d_j)} = \delta_{d(d_i l_j)}$, again independently of the chemical nature of the aggregate.[15] It is then obvious to predict that for a racemic mixture of l and d ($C_l = C_d$), $l_i d_j$ and $d_i l_j$ aggregates will form in equal amounts, and therefore $\delta_l = \delta_d$. On the other hand, in a mixture containing an excess of, say, l, $l_i d_j$ aggregates with $i > j$ will be preferentially

(14) *Molecular Association*; Foster, R., Ed.; Academic: New York, 1975; Vol. 1.

(15) In general, homochiral or heterochiral $l_i d_j$ ($i \neq j$) species will always be present as enantiomeric pairs. On the other hand, in a system undergoing fast exchange, $l_i d_j$ heterochiral species ($i = j$) admit at least one symmetric structure, i.e., C_i or C_2, which can correctly represent the whole system. Considering corresponding groups or atoms, "Chirotropic atoms located in chiral molecules are enantiotopic by external comparison between enantiomers. Chirotropic atoms located in achiral molecules are enantiotopic by internal and therefore by external comparison." Mislow, K.; Siegel, J. *J. Am. Chem. Soc.* **1984**, *106*, 3319–3328.

formed with respect to their $d_i l_j$ enantiomers; therefore, in general, $\delta_l \neq \delta_d$, and *two signals will be observed from a given nucleus in l and d molecules*. The separation of the two signals is expected to be a complicated function of the enantiomeric excess of l, of the formation constants of the various aggregates, of their chemical shift, and of the overall solute concentration $C_l + C_d$. However, from the fast-exchange condition and the above arguments, it follows that *the intensities of the two signals must always be proportional to the amount of l and d species in solution* (eq A6).

$$\frac{I_l}{I_d} = \frac{C_l}{C_d} \tag{A6}$$

II. Dimeric Systems. The experimental results obtained for dioxastannolanes can be discussed in the frame of the above general treatment.

On the basis of the available data,[7] the assumption can be made that the dioxastannolane systems are constituted only by dimeric species. Hence, eq A3 becomes

$$C_l = 2[l_2] + [ld] = 2[RR] + [RS] = C_R$$
$$C_d = 2[d_2] + [ld] = 2[SS] + [RS] = C_S \tag{A7}$$

and eq A4 and A5

$$\delta_R = \delta_{R(RR)}\frac{2[RR]}{C_R} + \delta_{R(RS)}\frac{[RS]}{C_R} = \frac{1}{C_R}(2\delta_{\text{homo}}[RR] + \delta_{\text{hetero}}[RS]) \tag{A8}$$

$$\delta_S = \delta_{S(SS)}\frac{2[SS]}{C_S} + \delta_{S(RS)}\frac{[RS]}{C_S} = \frac{1}{C_S}(2\delta_{\text{homo}}[SS] + \delta_{\text{hetero}}[RS]) \tag{A9}$$

where $\delta_{S(SS)} = \delta_{R(RR)} = \delta_{\text{homo}}$ and $\delta_{S(RS)} = \delta_{R(RS)} = \delta_{\text{hetero}}$. The difference in the chemical shifts of the two signals is therefore eq A10.

$$\Delta\delta = \delta_R - \delta_S = 2\delta_{\text{homo}}\left(\frac{[RR]}{C_R} - \frac{[SS]}{C_S}\right) + \delta_{\text{hetero}}\left(\frac{[RS]}{C_R} - \frac{[RS]}{C_S}\right) \tag{A10}$$

In order to predict δ_R and δ_S values, we shall express $[RR]$, $[SS]$, and $[RS]$ in terms of the analytical concentrations of R and S and of the constant (K) for the equilibrium $SS + RR \rightleftharpoons 2RS$ (eq A11).

$$K = \frac{[RS]^2}{[RR][SS]} \tag{A11}$$

Let X be the concentration of RR homodimers formed. Then

$$[RR] = X$$
$$[RS] = C_R - 2X$$
$$[SS] = X + (C_S - C_R)/2 \tag{A12}$$

and eq A11 becomes

$$K = \frac{(C_R - 2X)^2}{X^2 + X(C_S - C_R)/2} \tag{A13}$$

that can be written as

$$(K - 4)X^2 + X[KC_S + (8 - K)C_R]/2 - C_R^2 = 0 \tag{A14}$$

whose physically meaningful solution is

$$X = [K(C_S - C_R) + 8C_R - (K^2C_S^2 + K^2C_R^2 - 2K^2C_SC_R + 16KC_SC_R)^{1/2}]/4(4 - K) \tag{A15}$$

Substituting X into (A12) and the resulting equilibrium concentrations of dimers into (A8)–(A10), with some rearrangements, (A16) – (A18) are obtained.

$$\delta_R = \delta_{\text{hetero}} - \frac{2X}{C_R}(\delta_{\text{hetero}} - \delta_{\text{homo}}) \tag{A16}$$

$$\delta_S = \delta_{\text{homo}} - \left(\frac{2X}{C_S} - \frac{C_R}{C_S}\right)(\delta_{\text{hetero}} - \delta_{\text{homo}}) \tag{A17}$$

$$\Delta\delta = \delta_R - \delta_S = (C_R - 2X)\left(\frac{1}{C_R} - \frac{1}{C_S}\right)(\delta_{\text{hetero}} - \delta_{\text{homo}}) \tag{A18}$$

For $K = 4$,[13] (A15) becomes indeterminate. In such a case, X is immediately obtained by substituting 4 for K in (A14):

$$X = \frac{C_R^2}{2(C_R + C_S)} = f_R C_R/2 \tag{A19}$$

When X is substituted in (A16) – (A18) with some rearrangements and $C_R/C_S = 1/f_S - 1$, $f_S + f_R = 1$, and $f_S - f_R = \text{ee}$ are recalled, (A20)–(A22) are obtained.

$$\delta_R = \delta_{\text{hetero}} - f_R(\delta_{\text{hetero}} - \delta_{\text{homo}}) \tag{A20}$$

$$\delta_S = \delta_{\text{homo}} + f_R(\delta_{\text{hetero}} - \delta_{\text{homo}}) \tag{A21}$$

$$\Delta\delta = \delta_R - \delta_S = (\delta_{\text{hetero}} - \delta_{\text{homo}})\text{ee}/100 \tag{A22}$$

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