using (*S*)-(+)-valinol we were able to prepare (−)-grandisol meaning that utilization of (*R*)-(−)-valinol should lead to (+)-grandisol. This asymmetric methodology leading to chiral cyclobutanes is under active investigation.

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Supplementary Material Available: Isolation and complete physical data and NMR analysis using Mosher ester (7 pages). Ordering information is given on any current masthead page.

Self-Induced Nonequivalence in the Association of D- and L-Amino Acid Derivatives

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Consider enantiomerically enriched mixtures of chiral amino acid derivatives in achiral solvents. When the two enantiomers undergo diastereomeric solute–solute interactions to different extents, chiral differentiation of enantiomers may be possible without the aid of any foreign chiral substances since, by external comparison, each individual enantiomer can be in a different average environment.

In the present research, it was found that the enantiomeric *N*-acetylvaline *tert*-butyl ester (**1**)[1] exhibits self-induced NMR nonequivalence[2-4] through the formation of diastereomeric dimers interlinked via NH--O=C hydrogen bonds. Figure 1 illustrates two sets of amide NH proton doublets for D and L enantiomers recorded in a (0.1 M) CCl_4 solution at −20 °C. The intensity ratio of these signals was determined by the enantiomeric ratio in solution, indicating precisely that the associations occur under conditions of fast exchange. A similar chemical shift nonequivalence was also seen at higher sample temperatures as shown in Table I.

For a mixture of the enantiomers S_l and S_d, possible binary association equilibria are given as eq 1–3, where S_lS_l and S_dS_d

$$S_l + S_l \rightleftharpoons S_lS_l \qquad (1)$$

$$S_l + S_d \rightleftharpoons S_lS_d \qquad (2)$$

$$S_d + S_d \rightleftharpoons S_dS_d \qquad (3)$$

are a homochiral dimer and S_lS_d a heterochiral dimer, respectively. When S_l is in large excess, S_l is associated primarily according to eq 1 and S_d according to eq 2. When the binary associations occur under conditions of fast interassociate exchange and a chemical shift of the sensor nuclei in the homochiral dimer is different from that in the heterochiral dimer, two NMR signals due to the enantiomers can be obtained, one corresponding to the weighted average of the three signals from S_l, S_lS_d, and S_lS_l and the other corresponding to the weighted average of the three signals from S_d, S_lS_d, and S_dS_d. Thus, the chemical shift nonequivalence (Δδ) can be enhanced under conditions by which the enantiomeric purity of the enriched solute is enhanced. Decreasing the enantiomeric purity of the solute caused nonequivalent resonances to approach each other. In the 0.1 M racemic solution (C 0.5) in CCl_4, these resonances coalesced into one signal but with a chemical shift deviating by 0.051 ppm upfield from that of the corresponding L enantiomeric solution (homo shift).

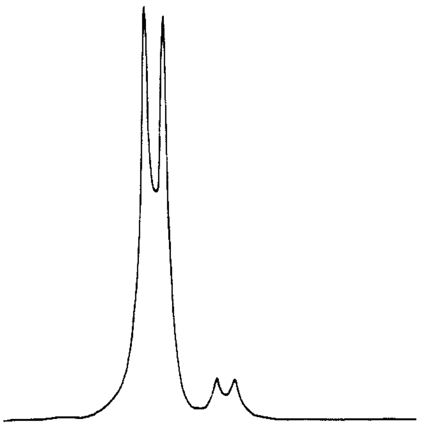

Figure 1. ^1H NMR spectrum of the amide NH group in the 1:9 mixture of D- and L-**1** (0.1 *M* solution in CCl_4) at −20 °C. The low-field doublet ($^3J_{HH}$ = 8.54 Hz, δ 6.725) and the small high-field doublet ($^3J_{HH}$ = 8.30 Hz, δ 6.566) were assigned to the L and D enantiomers, respectively, on the basis of an observed intensity ratio of 9:1.

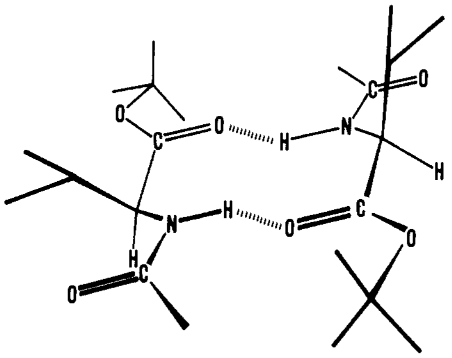

Figure 2. Proposed structure of the homochiral (L–L) dimer interlinked via bidentate NH--O=C ester hydrogen bonds.

A concentration study of ^1H and ^{13}C NMR in CCl_4 solution confirmed the involvement of the amide NH proton and each carbonyl carbon of both the ester and amide groups in hydrogen bond systems for both the pure enantiomer and racemic mixture. For the L enantiomer, the NH resonance shifted 0.38 ppm and the ^{13}C resonances for the two carbonyl carbons,[5] C=O amide and C=O ester, 0.43 and 0.22 ppm, respectively, upfield with dilution, in the concentration range 0.01–0.1 M (20 °C). Of the two carbonyl carbons, the resonance of the C=O ester carbon had a chemical shift difference between the racemic and L enantiomeric solution, similar to that observed for the amide NH resonance. In the 0.1 M racemic solution, the carbonyl ^{13}C resonance showed a weak but definite upfield shift of 0.05 ppm from that of the corresponding L enantiomeric solution. The chemical shift differences between the racemic and pure enantiomeric solution, observed in the resonances of the C=O ester carbon and that of the amide NH proton decreased with dilution in the above concentration region and finally disappeared at 0.01 M.

These results demonstrate that the association motifs of **1** contain two kinds of intermolecular hydrogen bonds: NH--O=C amide and NH--O=C ester. Of these two bonds, the sensor nuclei

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[1] *N*-Acetyl-L-valine *tert*-butyl ester, $[\alpha]^{18}_D$ −29.9° (*c* 1.00, ethanol) and its D enantiomer, $[\alpha]^{18}_D$ +29.6° (*c* 1.03, ethanol).

[2] Pirkle, W. H.; Hoover, D. J. Top. Stereochem. **1982**, *13*, 316. Five groups of chiral compounds for which self-induced NMR nonequivalence has been observed until now are cited therein.

[3] Williams, T.; Pitcher, R. G.; Bommer, P.; Gutzwiller, J.; Uskokovic, M. *J. Am. Chem. Soc.* **1969**, *91*, 1871.

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[5] Two carbonyl carbons of the solute **1** were assigned by using a selective proton-decoupling technique in ^{13}C NMR. Chemical shifts determined for C=O amide and C=O ester carbons at 20 °C are 170.90 and 167.55 ppm, respectively, for the L enantiomer (0.1 M solution in CCl_4).

Table I. Self-Induced Chemical Shift Nonequivalence ($\Delta\delta$) of the Amide NH Proton of **1** in (0.1 M) CCl$_4$ Solution[a]

	C[b]							
		0.9[c]			0.7[c]			
temp, °C	1.0	δ_L[d]	δ_D[d]	$\Delta\delta$[e]	δ_L[d]	δ_D[d]	$\Delta\delta$[e]	0.5[f]
20	6.127 (0)	0.011	0.097	0.086	0.028	0.071	0.043	0.051
0	6.389 (0)	0.010	0.143	0.133	0.032	0.098	0.066	0.073
−20	6.729 (0)	0.004	0.163	0.159	0.021	0.100	0.079	0.084

[a] NMR spectra were recorded at 200 MHz with Me$_4$Si (δ 0.00) as the internal standard. Chemical shifts of the amide NH doublets were determined by a homodecoupling technique, with irradiation of $^{\alpha}$H of the solute **1**. [b] Relative content of the L enantiomer in the mixtures. [c] Identical spectra were obtained in the reverse enantiomeric ratio (C of 0.1 for 0.9, C of 0.3 for 0.7), but assignment of the two lines has been reversed. [d] δ_D and δ_L values exhibit upfield deviation for the D and L enantiomers in enriched mixtures, respectively, from the homo shift of the pure L enantiomer (C 1.0). [e] $\Delta\delta = \delta_D - \delta_L$. [f] The sense of nonequivalence has vanished.

functioning to produce the latter bond showed a difference in the local magnetic environment, as was evident by a comparison of the racemic and pure enantiomeric solutions. This NH--O=C ester bond is thus a primary driving force for diastereomeric associations. We expect the observed sense of nonequivalence to be induced through formation of diastereomeric dimers in which associative interactions are the bidentate NH--O=C ester hydrogen bonds. Figure 2 illustrates a structure of the homochiral dimer (S$_l$S$_l$) as one of the diastereomeric dimers.

The magnitude of self-induced nonequivalence ($\Delta\delta$) was enhanced dramatically with a decrease in sample temperature. This means that lower temperatures cause an increase in the fractional population of diastereomeric species in self-association equilibria. The chemical shift deviation from the homo shift (δ_L) in the NH resonance assigned to the L enantiomer in enriched mixtures increased linearly while that of the D enantiomer (δ_D) decreased linearly with a decrease in C values at 20 °C, as evident from Table I. This linear δ–C relationship indicates the proportion of homochiral or heterochiral dimers to certainly be under statistical control.[6] An increase in $\Delta\delta$ while lowering the temperature was accompanied, however, by deviation from this linearity and the δ–C relationship gave a concave line approaching the homo shift at each temperature. This behavior reflects the existence of additional stability imparted to the homochiral dimer in diastereomeric associations and, by virtue of the difference in their stabilities, an enhancement of differences in the fractional populations of these species at lower temperatures. The linear δ–C relationships obtained at 20 °C thus suggest that the association stereoselectivity explicitly observed at lower temperatures is still dormant at this temperature. IR spectra confirmed this stability difference in diastereomeric dimers. L-Enantiomeric solutions provide stronger intensities of the hydrogen-bonded NH stretching band (3360 cm^{-1})[7] in their amide groups than those in the racemic mixtures at concentrations greater than 0.01 M in CCl$_4$ (ca. 23 °C).[8]

The NMR spectra of unequal mixtures of the congener *N*-acetylvaline ethyl ester (**2**) in CCl$_4$ revealed no chemical shift nonequivalence at 20 °C. Lower sample temperatures had little effect on the shift difference between the D and L enantiomers of **2** in the enriched mixtures, which was as high as 0.078 ppm even for an enantiomeric ratio of 1:9 (0.1 M) at −20 °C. The marked reduction in the magnitude of $\Delta\delta$ by substitution of the *tert*-butyl with an ethyl group demonstrates that the chemical shift nonequivalence observed for the chiral solute **1** depends strongly on the steric bulkiness of *tert*-butyl substituent. It appears likely that steric bulkiness contributes to preponderant dimer formation in self-association equilibrium as well as imparts greater intrinsic magnetic nonequivalence between the nuclei of diastereomeric dimers.

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Registry No. L-**1**, 75552-82-8; D-**1**, 75552-81-7; L-**2**, 2382-78-7; D-**2**, 92998-92-0.

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[8] Optically active and racemic **1** samples showed stretching vibration of hydrogen-bonded NH as well as that of nonhydrogen-bonded NH (3460 cm^{-1}) in their amide groups at concentrations greater than 0.01 M: Abs(bonded NH)/Abs(nonbonded NH) = 2.5/7.2 for the L enantiomer and 2.0/7.15 for the racemate in (0.1 M) CCl$_4$ solution.

[9] *N*-Acetyl-L-valine ethyl ester, $[\alpha]^{30.5}_{D}$ −30.8° (*c* 1.00, ethanol) and its D enantiomer $[\alpha]^{30.5}_{D}$ +30.2° (*c* 1.00, ethanol).

A Novel Photocatalytic Process of Amine N-Alkylation by Platinized Semiconductor Particles Suspended in Alcohols

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Among many reactions being photocatalyzed by suspended semiconductor particles, several processes are applicapable to synthesis in organic solvents.[1-7] Our recent report has demonstrated the preparation of symmetrical secondary amines from primary amines using photocatalysis by platinized titanium dioxide (TiO$_2$/Pt) suspension in water.[8] The present paper describes photocatalytic preparation of unsymmetrical secondary and tertiary amines by TiO$_2$/Pt suspended in a variety of alcohols as solvents. The alcohols were potent N-alkylation reagents, in contrast to the aqueous system in which the substrate amines acted as N-alkylation reagents. This N-alkylation proceeds efficiently at room temperature, providing an advantage over the thermal catalytic processes by nickel,[9] rhodium,[10] and ruthenium.[11-13]

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