any soluble impurities. Suspension of 7 in an ether or hydrocarbon solvent followed by *n*-butyllithium addition and shaking at room temperature overnight led to formation of the purplish polymer 8.

Analysis of Polymers 1, 3-6, and 8. The loading of organometallic species on these polymers was estimated on the basis of the amount of soluble base detected in an acid-base titration of a methanol quench of known amounts of these polymers. In these analyses, the organometallic polymers were typically washed with dry THF until the THF washes contained no basic species in order to remove any soluble bases that might be present. In such cases, addition of THF to the solid organometallic polymer formed suspensions of polymer that contained no soluble base as determined by acid-base titration of aliquots of the solutions over these polymers. Addition of these suspensions to excess methanol produced methoxide base, which was subsequently titrated with standardized HCl to a phenolphthalein endpoint.

General Procedure for Deprotonation Reactions. A weighed amount of polymer (ca. 2 g) was placed in a flame-dried flask under a nitrogen atmosphere and swollen with ca. 12 mL of THF, and the resulting suspension of swollen polymer was then cooled to -78 °C. Deprotonation with *n*-BuLi as described above followed by washing with THF until no excess soluble base was detected in the washes produced 1, which was then used for a deprotonation reaction. Addition of 10 mL of THF and cooling of the polymer suspension to -78 °C followed by addition of 0.25 mmol of a weak carbon acid substrates and 2 h of stirring (at -78 °C for ketones to produce the desired enolate and at room temperature for fluorene) yielded a solution of the desired stabilized carbanion. In the case of deprotonation of a ketone substrate, transfer of the enolate solution formed in this fashion from the flask containing the polymer to a separate flask at -78 °C followed by addition of excess methyl iodide led to formation of methylated product whole yield was determined by GC relative to an internal hydrocarbon standard. Fluorene anion was detected by UV-visible spectroscopy, by titration of the organometallic species in solution and by ^{13}C NMR spectroscopic analysis of the product of a deuterium oxide quench.

Acknowledgment. Support of this research by the Office of Naval Research and the Texas A&M Center for Energy and Mineral Resources is gratefully acknowledged.

Registry No. Fluorene, 86-73-7; 2-butanone, 78-93-3; 3,3-dimethylbutanone, 75-97-8; acetophenone, 98-86-2; camphor, 76-22-2.

A Method for the Determination of the pK_a of the α-Hydrogen in Amino Acids Using Racemization and Exchange Studies

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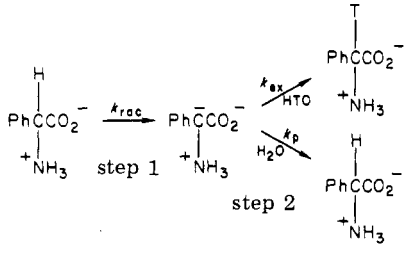
A mechanism for the racemization of amino acids, which was recently reported in this journal by Smith and Sivakua,[1] is shown below: The absence of a kinetic isotope



effect in step 2, as evidenced by the rate of reprotonation (k_p) equaling that of tritium exchange (k_{ex}), indicated that step 1, abstraction of the methine hydrogen, is the rate-controlling step. We are now reporting another racemization study, focusing on step 1, which shows that this step does display a kinetic isotope effect with a k_H/k_D value of 2.0 (Figure 1). This indicates that deprotonation is indeed the slower, rate-controlling step. A new exchange study, using deuterium oxide instead of tritiated water, confirms that step 2, of the above mechanism, is not influenced by the strength of bond reformation (Figure 2). Similar findings have previously been reported.[2,3] In view of these data, it seems reasonable to assume that step 2 is predominantly a diffusion-controlled process and that the rate of reprotonation (k_p) can be assumed to be equal to the diffusion-controlled rate (k_d) in the solvent.

If this mechanism is valid, it should allow the calculation of the pK_a of the α-hydrogen of any amino acid, for which k_{rac} has been determined, via eq 1. Calculations of the

$$pK_a = -\log k_{rac}/k_d \quad (1)$$

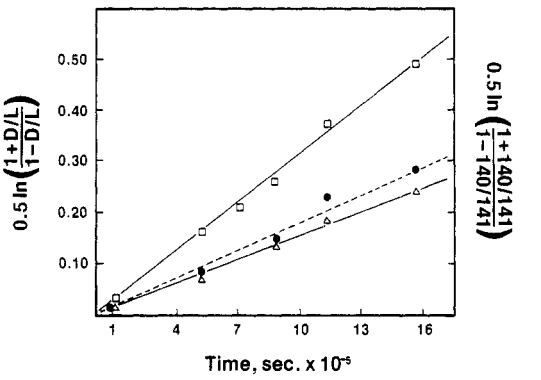


Figure 1. Rate of racemization L (left ordinate) and rate of exchange (right ordinate) of L-alanine-2-*H* and L-alanine-2-*d*: (□) H, (△ D, and (●) exchange.

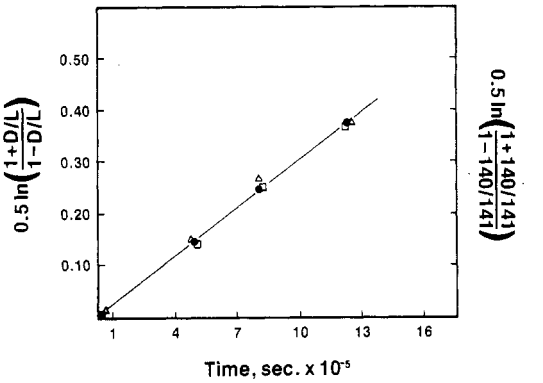


Figure 2. Rate of racemization (left ordinate) and rate of exchange (right ordinate) of L-alanine-2-*H* in D_2O and H_2O: (□) H_2O, (△) D_2O, and (●) exchange.

Table I. α-Hydrogen pK_a Values

amino acid	$10^7 k_{rac}$,[a,b] s^{-1}	pK_a
alanine	17.7	16.5
valine	5.9	17.0
isoleucine	7.8	16.9
leucine	11.7	16.7
phenylalnine	34.8	16.2
D-phenylglycine	788.8	14.9

[a] Determined at 139.0 °C, pH 7.6 in 0.05 M NaH_2PO_4. $k_d = 6 \times 10^{10}$ M^{-1} s^{-1}. [b] Reference 1.

(1) Smith, G. G.; Sivakua, T. *J. Org. Chem.* **1983**, *48*, 627.

(2) Matsuo, H.; Kawazoe, Y.; Sato, M.; Ohnishi, M.; Tatsuno, T. *Chem. Pharm. Bull.* **1967**, *15*, 391.

(3) Matsuo, H.; Kawazoe, Y.; Sato, M.; Ohnishi, M.; Tatsuno, T. *Chem. Pharm. Bull.* **1970**, *18*, 1788.

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Table II. Comparison of Calculated ΔG° and Literature E_a

amino acid	ΔG°	E_a (kcal mol^{-1}) Bada[a]	Dungworth[b]	Smith et al.[c]
alanine	31.1	30.9	29.4	28.5
valine	32.0		29.1	28.6
isoleucine	31.9	31.4	28.9	27.9
leucine	31.5		29.3	27.7
phenylalanine	30.6	28.6		24.0
D-phenylglycine	28.1			

[a] Bada, J. L. *Adv. Chem. Ser.* **1971**, *No. 106*, 309. [b] Dungworth, G.; Vincken, N. J.; Schwartz, A. W. In Tissot, B.; Bienner, F. *Adv. Inorg. Chem.* **1973**, 689. [c] Smith, G. G.; Williams, K. M.; Wonnacott, D. M. *J. Org. Chem.* **1978**, *43*, 1.

k_d and pK_a values for a variety of amino acids are reported in Table I. Generally, k_{rac} values are determined at elevated temperatures due to the relatively slow rate of racemization at room temperature. These values are readily available in the literature for a variety of amino acids and reaction conditions.[1] It must be noted that racemization at basic pH is general base catalyzed, thus necessitating accurate knowledge of pH and buffer concentration when determining or comparing pK_a values.[1]

The k_d value is dependent upon both the temperature at which the k_{rac} was determined and the viscosity of the solvent, according to eq 2,[4] where η is viscosity. Viscosity

$$k_d = 8RT/2000\eta \quad (2)$$

is inversely proportional to the solution temperature and can be calculated at a specific temperature from empirical relationships derived from viscosity measurements.[5] It is assumed that pressures greater than 1 atm do not have a significant effect upon the k_d calculation.

An assessment of the validity of the assumption that the reprotonation is predominantly diffusion controlled can be made by calculating ΔG° from the pK_a values obtained using k_d (Table I) via the equation $\Delta G^\circ = 2.303RTpK_a$. ΔG° should be equal to the energy of activation (E_a) since we assumed no energy barriers in the reprotonation step. Table II shows ΔG° calculated from the pK_a values in comparison to literature E_a values. The close agreement of these values indicates that this simple calculation (eq 1), from existing racemization data, provides a good estimate of the α-hydrogen pK_a and E_a for amino acids and further substantiates the Smith–Sivakua mechanism for amino acid racemization.

Experimental Section

An HP5830A gas chromatograph, equipped with an FID detector, was used to determine the D/L configuration of the amino acids. The isotope-exchange studies employed an LKB 2091 gas chromatograph–mass spectrometer interfaced to a PDP 11-03 data system.

Racemization (Figure 1) and Derivatization Procedure. L-Alanine-*2-H* and L-alanine-*2-d* (MSD Isotopes, 98 atom % D) were dissolved in 0.05 M NaH_2PO_4 buffer to give a 0.02 M solution of pH 8.7. Aliquots (1.0 mL) were sealed in glass tubes and heated at 121.7 °C for six time periods ranging from 0 to 20 days. Samples were evaporated to dryness under a stream of N_2. 2-Propanol–4 N HCl (1.5 mL) was added. The tubes were sealed and heated at 110 °C for 2 h to effect esterification. The excess 2-propanol was evaporated as above, and 1.5 mL of 30% trifluoroacetic anhydride–methylene chloride was added. The solution remained at room temperature for 45 min, after which the excess reagent was evaporated to produce the *N*-(trifluoroacetyl)amino acid isopropyl ester derivative.

Exchange Experiment (Figure 2). L-Alanine-*2-H* was dissolved in D_2O to produce a 0.02 M solution. A control of L-alanine-*2-H* in H_2O was identically prepared. Both were heated and derivatized as described above.

Sample Analysis. Gas Chromatography. The derivatized samples were dissolved in 0.5 mL of CH_2Cl_2 and 1.0-μL aliquots were analyzed for D/L by GC. A stainless steel capillary column (150 ft × 0.02 in.) coated with a 1/1 mixture of *N*-octadecanoyl-L-valyl-L-valylcyclohexyl ester and *n*-docosanoyl-L-valyl-*tert*-butylamide was used. Base-line resolution of the D and L isomers was obtained in all analyses.

Mass Spectroscopy. The L-alanine-*2-d* and L-alanine-*2-H* (in D_2O) samples were analyzed for exchange. With use of the same column described above, the samples were resolved to their D and L isomers, and the mass spectrum of each was recorded. Exchange was calculated as a ratio of the absolute intensity of ions 140 to 141 in the L isomer. These values were corrected by an unracemized L-alanine-*2-d* control (in the racemization experiment of Figure 1) and by an unracemized L-alanine-*2-H* control (in the exchange experiment of Figure 2). A derivation of the amino acid racemization equation used in plotting Figures 1 and 2 may be found in ref 7.

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Registry No. L-Alanine, 56-41-7; L-valine, 72-18-4; L-isoleucine, 73-32-5; L-leucine, 61-90-5; L-phenylalanine, 63-91-2; D-phenylglycine, 875-74-1; L-alanine-*2-d*, 21386-65-2.

(4) Murov, S. L. "Handbook of Photochemistry"; Marcel Dekker: New York, 1973; p 55.
(5) "Handbook of Chemistry and Physics", 62nd ed.; CRC Press: Boca Raton, FL, 1981; p F-42.
(6) Wonnacott, D. M. Ph.D. Thesis, Utah State University, Logan, UT, 1979.
(7) Williams, K. M.; Smith, G. G. *Origins Life* **1977**, *8*, 91.

Asymmetric Strecker Synthesis: Isolation of Pure Enantiomers and Mechanistic Implications

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The current direction in organic synthesis toward biologically active asymmetric compounds has been stimulated by advances in asymmetric syntheses. Though recently developed reagents for asymmetric induction have resulted in increasingly higher optical yields, few reactions have afforded pure enantiomers,[1] the ultimate goal of an asymmetric synthesis. We herein report results of our research on the Strecker reaction whereby aliphatic and aromatic aldehydes are isolated as pure chiral amino nitriles of either absolute configuration in acceptable synthetic yields. The ease of synthesis and isolation of these highly functionalized compounds makes them attractive starting materials for the synthesis of more complex molecules of biological interest. In addition, the asymmetric center provides information as to the mechanism of the Strecker reaction.

The asymmetric Strecker synthesis has been known for nearly 2 decades,[2] though it has been utilized primarily in the synthesis of chiral amino acids. The isolation of chiral

(1) For a review of recent advances in asymmetric synthesis see: Ap-Simon, J.; Seguin, R. *Tetrahedron*, **1979**, *35*, 2797.
(2) Harada, K. *Nature (London)* **1963**, *200*, 1201.

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