and k_{-2} and the $k_1{:}k_2$ ratio of 4.6 may be calculated from the proportions of the two alcohols produced in the cleavage process. These results indicate a clear preference for the [2,3]-sigmatropic process to proceed across the equatorial face of the cyclohexylidine ring system producing predominately the less stable equatorial alcohol **9b**.[17] This stereochemical outcome is consistent with a reactant-like transition state where steric effects are the major factors governing product geometry.[18]

The use of less efficient thiophiles for the interception of sulfenate esters **9a** and **10a** results in a change in the ratio of allylic alcohols produced when k_e and k_a approach the values of k_{-1} and k_{-2}. The results in Table II confirm this prediction.

Table II. Effect of Thiophile on **9b**:**10b** Ratio at 25° in Methanol[a]

Thiophile [T]	**9b**:**10b**	% conversion
$LiBH_3CN$	58:42	24
Piperidine	66:34	90
$C_6H_5S^-$	88:12	99
$[(C_2H_5)_2N]_3P$	92:8	99
$(CH_3O)_3P$	92:8	99

[a] All reactions were carried out with a 10:1 excess of thiophile for 14 days at 25°.

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(17) From ref 13, **10b** is calculated to be 0.64 kcal/mol more stable than **9b** at 38°.

(18) M. Chérest and H. Felkin, *Tetrahedron Lett.*, 2205 (1968).

(19) Camille and Henry Dreyfus Teacher-Scholar recipient, 1971–1976.

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Medium Activity Coefficient of Silver Cation between Acetonitrile and Water

Sir:

We have drawn attention[1] to some of the problems in estimating a number which is important to chemists, the medium activity coefficient, log ${}^{An}\gamma^{W}_{Ag^+}$ for transfer of silver cation from acetonitrile to water at 25°. Kolthoff and Chantooni[2] have removed one of these problems by measuring the solubility product (pK_s = 17.2) of silver tetraphenylboride in water at 25°. We have measured some solubilities and equilibrium constants which give us confidence that log ${}^{An}\gamma^{W}_{Ag^+}$ is between 3 and 4.

The solubility (S, moles liter^{-1}) of tetraphenylmethane is $10^{-7.8}$ in water and $10^{-3.2}$ in acetonitrile.[1] The new value for water was found by ether-extracting 1 l. of a saturated solution of tetraphenylmethane in water containing triphenylmethane, added as internal standard after saturation and filtering. The ether extract was evaporated to 0.5 ml and analyzed by gas chromatography on a SE-30 column at 250° using a flame ionization detector.

The solubility product, $pK_s^W(Ph_4AsBPh_4)$, of tetraphenylarsonium tetraphenylboride in water at 25° is 17.4[3] (molar scale). In acetonitrile, $pK_s^{An}(Ph_4AsBPh_4)$ is 6.0. The new value for water is the mean of 17.3 and 17.5 measured (a) by equilibrating (eq 1) 50 ml of

$$Ph_4AsBPh_4\downarrow + AgNO_3 \rightleftharpoons Ph_4AsNO_3 + AgBPh_4\downarrow \quad (1)$$

0.01 *M* silver nitrate with 1 g of Ph_4AsBPh_4 containing a trace of $AgBPh_4$ as seed and (b) by equilibrating 50 ml of 0.01 *M* Ph_4AsNO_3 with 1 g of $AgBPh_4$ containing a trace of Ph_4AsBPh_4 as seed. Methods a and b both gave 6.0 for $pK_s^{An}(Ph_4AsBPh_4)$.[4] Equilibration was in CO_2-free water or anhydrous acetonitrile, under nitrogen by shaking in lightproof vessels. The solutions were analyzed for silver by atomic absorption and for Ph_4As^+ by its uv absorption at 265 mμ. Equation 2 gave $pK_s(Ph_4AsBPh_4)$ using $pK_s^W(AgBPh_4)$ = 17.2[2]

$$pK_s(Ph_4AsBPh_4) = [Ph_4As^+]/[Ag^+] + pK_s(AgBPh_4) \quad (2)$$

and $pK_s^{An}(AgBPh_4)$ = 7.6,[5] respectively. Equation 2 also gave $pK_s^W(AgBPh_4) - pK_s^W(Ph_4AsBPh_4) = -0.2$ and $pK_s^{An}(AgBPh_4) - pK_s^{An}(Ph_4AsBPh_4) = 1.6$.

The latter value compares favorably with 1.7 calculated from our previously reported $pK^{An}(Ph_4AsBPh_4) = 5.8$ and $pK_s^{An}(AgBPh_4) = 7.5$ at zero ionic strength.

Values of log ${}^{An}\gamma^{W}_{Ag^+}$ are in Table I. Four of them are from other assumptions, as reported previously.[1] They are compared with the three new values calculated from the solubility products of $AgBPh_4$, Ph_4AsBPh_4, and Ph_4C in water and acetonitrile by assuming (i) that ${}^{An}\gamma^{W}_{Ph_4As^+} = {}^{An}\gamma^{W}_{Ph_4B^-}$; (ii) that ${}^{An}\gamma^{W}_{Ph_4B^-} = {}^{An}\gamma^{W}_{Ph_4C}$; and (iii) that ${}^{An}\gamma^{W}_{Ph_4As^+} = {}^{An}\gamma^{W}_{Ph_4C}$ in eq 3. In eq 3 the concentrations of Ag^+

$$\log {}^{An}\gamma^{W}_{Ag^+} = \log \frac{[Ag^+]^W}{[Ph_4As^+]^W} - \log \frac{[Ag^+]^{An}}{[Ph_4As^+]^{An}} + pS^W Ph_4C - pS^{An} Ph_4C \quad (3)$$

and Ph_4As^+ in water and acetonitrile are those prevailing at equilibrium in reaction 1 and thus the first two

Table I. Values of Log ${}^{An}\gamma^{W}_{Ag^+}$ (Molar Scale) at 25°

Assumption[a]	Log ${}^{An}\gamma^{W}_{Ag^+}$	Assumption[a]	Log ${}^{An}\gamma^{W}_{Ag^+}$
${}^{An}\gamma^{W}_{Ph_4As^+} = {}^{An}\gamma^{W}_{Ph_4B^-}$	3.9[b]	Negligible E_{1j}	3.1[c]
${}^{An}\gamma^{W}_{Ph_4As^+} = {}^{An}\gamma^{W}_{Ph_4C}$	2.8[b]	${}^{An}\gamma^{W}_{\ddagger^-}$	3.2[c]
${}^{An}\gamma^{W}_{Ph_4B^-} = {}^{An}\gamma^{W}_{Ph_4C}$	5.0[b]	${}^{An}\gamma^{W}_{ArF} = {}^{An}\gamma^{W}_{\ddagger^{*-}}$	2.8[c]
		${}^{An}\gamma^{W}_{Fc} = {}^{An}\gamma^{W}_{Fc^+}$	6.1[c]

[a] Abbreviations: Ar = 4-nitrophenyl; $\ddagger^-$ is the transition state anion for the SN2 reaction of SCN^- with CH_3I; $\ddagger^{*-}$ is the transition state anion for the SNAr reaction of N_3^- with ArF; Fc is ferrocene; Fc^+ is ferricinium cation. [b] This work. [c] Reference 1.

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(1) R. Alexander, A. J. Parker, J. H. Sharp, and W. E. Waghorne, *J. Amer. Chem. Soc.*, **94**, 1143 (1972).

(2) I. M. Kolthoff and M. K. Chantooni, *Anal. Chem.*, **44**, 194 (1972).

(3) I. M. Kolthoff and M. K. Chantooni, *J. Amer. Chem. Soc.*, **93**, 7104 (1971), calculated a value of 17.3 from solubility products of a variety of salts.

(4) A direct measurement[1] on a saturated solution of Ph_4AsBPh_4 in acetonitrile gave pK_s^{An} = 5.8.

(5) This is a mean value between 7.5 from ref 1 and 7.7 from I. M. Kolthoff and M. K. Chantooni, private communication.

terms on the right of eq 3 are equivalent to log ${}^{An}\gamma^{W}_{Ag^+}$ − log ${}^{An}\gamma^{W}_{Ph_4As^+}$ or log K^{An}/K^{W}, where K is the equilibrium constant for (1). It will be noted that eq 3 is independent of the solubility product of $AgBPh_4$ and Ph_4AsBPh_4 and does not require corrections for Debye–Hückel salt effects. The value of log ${}^{An}\gamma^{W}_{Ag^+} = 2.8$ from this cation–molecule assumption compares unfavorably with our value of 6.1[1] by applying Strehlow's ferricinium cation, ferrocene molecule assumption to polarographic data. Table I encourages us to accept a value of between 3 and 4 for log ${}^{An}\gamma^{W}_{Ag^+}$ and to recommend the value of 3.9, which follows from the cation–anion assumption that ${}^{An}\gamma^{W}_{Ph_4B^-} = {}^{An}\gamma^{W}_{Ph_4As^+}$. Thus we are now in close agreement with Kolthoff[3] and Popovych[6] as to an acceptable assumption for single ion medium activity coefficients for transfer from water.

(6) O. Popovych, *Crit. Rev. Anal. Chem.*, **1**, 73 (1970).

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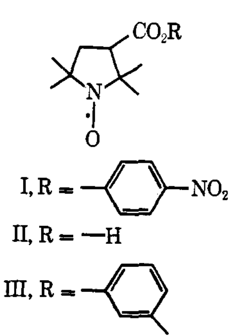
Enantiomeric Specificity in the Chymotrypsin-Catalyzed Hydrolysis of 3-Carboxy-2,2,5,5-tetramethylpyrrolidin-1-oxy *p*-Nitrophenyl Ester

Sir:

Enantiomeric specificity is an important property of enzyme-catalyzed reactions which has been studied extensively in the chymotrypsin-catalyzed reactions of many substrates. However, there is a dearth of quantitative information comparing the relative magnitudes of the individual rate parameters for both enantiomers of asymmetric substrates which are hydrolyzed by chymotrypsin according to the general scheme of eq 1. We wish now to report our measurements of these kinetic parameters for the chymotrypsin-catalyzed hydrolysis of both enantiomers of the spin-labeled chiral nonspecific ester substrate 3-carboxy-2,2,5,5-tetramethylpyrrolidin-1-oxy *p*-nitrophenyl ester.[1-3]

$$E + S \underset{K_s}{\rightleftharpoons} E\cdot S \xrightarrow{k_2} ES' + P_1 \xrightarrow{k_3} E + P_2 \qquad (1)^{4,5}$$



The racemic acid II was resolved using α-methylbenzylamine in acetone. The dextrorotatory isomer of II, prepared using L(−)-α-methylbenzylamine, has mp 205–207°, $[\alpha]^{25}D$ +79 ± 1° (EtOH). The levorotatory isomer of II, prepared using (+)-α-methylbenzylamine, has mp 203–205°, $[\alpha]^{25}D$ −81 ± 2° (EtOH). The (+) and (−) isomers of ester I were prepared by coupling the corresponding isomers of the acid II to *p*-nitrophenol with dicyclohexylcarbodiimide.[1]

From visible absorption measurements of the rate of release of *p*-nitrophenolate from (+)- or (−)-I at 25° in pH 7.0 phosphate buffer, $\mu = 0.5$, in 1% CH_3CN, with varying amounts of excess chymotrypsin, values of $K_s = (5.1 \pm 1.2) \times 10^{-4}\ M$ and $k_2 = (4.1 \pm 0.5) \times 10^{-2}\ sec^{-1}$ were calculated for the acylation of the enzyme by (−)-I, and values of $K_s = (4.1 \pm 0.4) \times 10^{-4}\ M$ and $k_2 = 0.37 \pm 0.02\ sec^{-1}$ were calculated for the reaction of (+)-I. From similar measurements of rates of *p*-nitrophenolate release in the presence of excess (+)- or (−)-I, values of $k_3 = (2.5 \pm 0.3) \times 10^{-4}\ sec^{-1}$ for the acyl enzyme derived from the reaction of (−)-I with chymotrypsin, and $k_3 = (5.2 \pm 0.2) \times 10^{-3}\ sec^{-1}$ for the acyl enzyme derived from (+)-I and chymotrypsin, were calculated. Thus, the enantiomeric specificity of the k_3 step of the chymotrypsin-catalyzed hydrolysis of I is greater than that of the k_2 step.

Solutions of the acyl enzymes derived from (+)- or (−)-I and chymotrypsin were prepared in analogy with the method of Berliner and McConnell[1] by allowing the *p*-nitrophenyl ester to react with chymotrypsin in pH 4.8 acetate buffer. The acyl chymotrypsin was separated from acid II, *p*-nitrophenol, and unreacted ester by filtration through G-15 Sephadex using pH 2.4 phosphate buffer, $\mu = 0.3$. The esr spectra of solutions of the two diastereomeric acyl enzymes prepared in this way are similar and characteristic of "strongly immobilized" spin labels. By raising the pH of each acyl enzyme solution to 6.9–7.3 and following the increase in height of the high-field line of the esr spectrum of acid II with time, values of $k_3 = (2.3 \pm 0.2) \times 10^{-4}\ sec^{-1}$ for release of (−)-II and $k_3 = (4.5 \pm 1.0) \times 10^{-3}\ sec^{-1}$ for release of (+)-II were determined. These values do not differ significantly from the values for k_3 determined by visible absorption spectroscopy.

In an attempt to examine the nature of the noncovalent binding of (+)- and (−)-I to the enzyme, the interaction of the two isomers of I with chymotrypsin at pH 2.3, where the chymotrypsin-catalyzed release of *p*-nitrophenol from the esters is very slow, was also studied. Measurements of K_s by the method of equilibrium dialysis at 0 and 15°, followed by extrapolation to 25°, gave values of $K_s = 4 \times 10^{-3}\ M$ for either isomer of I at pH 2.3 in HCl–KCl solution, $\mu = 0.08$, in 1% CH_3CN. Addition of $1.1 \times 10^{-3}\ M$ chymotrypsin to a $5 \times 10^{-5}\ M$ solution of either isomer of I in the pH 2.3 HCl–KCl mixture caused a small change in the shape of the solution's esr spectrum, corresponding to an approximately twofold increase in average rotational correlation time.[6] The small increase in correlation time cannot be accounted for by the increase in viscosity on addition of the enzyme, and, presumably, is due to

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(1) L. J. Berliner and H. M. McConnell, *Proc. Nat. Acad. Sci. U. S.*, **55**, 708 (1966).

(2) L. J. Berliner and H. M. McConnell, *Biochem. Biophys. Res. Commun.*, **43**, 651 (1971).

(3) E. J. Shimshick and H. M. McConnell, *ibid.*, **46**, 321 (1972).

(4) M. L. Bender and F. J. Kézdy, *Annu. Rev. Biochem.*, **34**, 49 (1965).

(5) In eq 1, E represents the enzyme, S the substrate, E·S the Michaelis complex, ES′ the acyl enzyme, P_1 the product alcohol, and P_2 the product acid.

(6) D. Kivelson, *J. Chem. Phys.*, **27**, 1087 (1957); J. H. Freed and G. K. Fraenkel, *ibid.*, **39**, 326 (1963).