Micelle-Induced Changes in the Solvation of Carbocations: Effect of Sodium Dodecyl Sulfate Micelles on the Enantiomer-Specific Oxygen Exchange Reactions of 1-Phenyl-1-ethanol and 1-Phenyl-1-butanol

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Abstract: The enantiomer-specific oxygen exchange rate constants of 1-phenyl-1-ethanol (**1**) and 1-phenyl-1-butanol (**2**) as a function of the change in configuration at the chiral center in micellar sodium dodecyl sulfate (SDS) at 64.5 ± 0.5 °C have been determined and found to differ from their values in nonmicellar media. Addition of 0.1 M SDS to the aqueous reaction media reduces the overall rate of racemization and selectively alters the enantiomer-specific oxygen exchange reactions with the solvent for both alcohols. Although the rate constant for oxygen exchange of the C1 hydroxyl with the solvent with inversion of configuration, k_{EI}, decreases to the same extent as that for the overall racemization, that for exchange with retention, k_E, increases markedly in SDS media. For **1** in water, k_E/k_{rac} = 0.35 ± 0.05; in 0.1 M SDS, k_E/k_{rac} = 0.63 ± 0.01. For **2** in water, k_E/k_{rac} = 0.47 ± 0.03; in 0.1 M SDS, k_E/k_{rac} = 1.67 ± 0.04. The larger effect of SDS on the reactions of **2** reflects the larger association constant, K_{assoc}, between this alcohol and micellar SDS: K_{assoc} = (5.7 ± 0.7) × 10^2 for **2** and (1.3 ± 0.1) × 10^2 for **1**. A 60% reduction of ^{1}H NMR longitudinal relaxation times, T_1, for the methyl protons of both 1-phenylalkanols by 0.1 M SDS is consistent with the alcohols being in a more constrained environment in micellar media than in unorganized media. Although the kinetic results suggest that micellar SDS strongly perturbs the solvation sphere of the intermediate carbocations, the identity of the ^{1}H NMR chemical shifts of **1** and **2** in water and in 0.1 M SDS indicates, however, that the polarity of this microenvironment is similar to that of water.

The rates of ^{18}O exchange between the solvent and optically active alcohols have provided evidence for the participation of ion–molecule pairs[1-14] in the racemization of optically active alcohols. In these reactions, the species analogous to the intimate (contact) ion pair of solvolysis reactions[15] is a carbocation–water complex formed from the initially formed carbocation paired with the departing water. The nature and dynamics of solvation of these ion–molecule pairs have been revealed by analysis of the rate constants for three competing processes at the chiral center in the acid-catalyzed racemization of 1-phenyl-1-ethanol (**1**),[12,13] 1-phenyl-1-butanol (**2**),[13] and 1-phenyl-1-propanol (**3**)[13] in isotopically distinct water: (1) substitution (hydroxy O exchange with water) with retention at the chiral center, k_E, (2) substitution (hydroxy O exchange with water) with inversion, k_{EI}, and (3) inversion without substitution, k_I:

$$\mathbf{R} \overset{k_E}{\rightleftharpoons} \mathbf{R}', \text{ oxygen exchange with retention} \quad (1)$$

$$\mathbf{R} \overset{k_{EI}}{\rightleftharpoons} \mathbf{S}', \text{ oxygen exchange with inversion} \quad (2)$$

$$\mathbf{R} \overset{k_I}{\rightleftharpoons} \mathbf{S}, \text{ inversion without oxygen exchange} \quad (3)$$

R symbolizes the optically pure starting material and **R′** the same isomer in which the original oxygen has been replaced with that of the solvent. Similarly, **S** and **S′** symbolize the isomer with inverted configuration relative to the starting material and contain either the oxygen of the starting material or that of the solvent, respectively. The two oxygen exchange reactions (eqs 1 and 2) each involve the incorporation of an isotopically distinct solvent oxygen into the specified alcohol isomer. For these three alcohols, it was found that the last process (similar to internal return in solvolysis reactions) in which the departing water remains associated with the carboca-

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tion intermediate (an ion−molecule pair) and attacks this species from the opposite face made the same small, 1−3%, but significant contribution to the change in stereochemistry at C1. In contrast, the three 1-phenylalkanols differed in the relative contributions of the two oxygen exchange reactions with the solvent to the racemization process: **3** behaved similarly to **1** in that $k_E < k_{EI}$, whereas, for **2**, $k_E \approx k_{EI}$.

An ion−molecule pair composed of the initially formed carbocation and the departing water is central to the common mechanism proposed to account for these variations. In this proposed mechanism, variations in the rate constants for the oxygen exchange reactions can be accounted for by differences in the relative rates at which the departing water equilibrates with water molecules within the solvation sphere of these intermediates and with the bulk solvent. As the size of the alkyl substituent at the chiral center increases from methyl to propyl, the departing water appears to be less tightly associated with the intermediate carbocation as k_E approaches k_{EI}. In the case of **2**, the near equality of the two rate constants is consistent with rapid equilibration of the departing water with the bulk solvent. This observed dependence of the enantiomer-specific oxygen exchange rate constants on the alkyl substituent at the chiral center indicates that they are sensitive indicators of the structure and dynamics of the solvation sphere of the carbocation.

The utility of enantiomer-specific oxygen exchange reactions in revealing details of carbocation solvation was shown by earlier studies of the epimerization of the 15-methylprostaglandins which found that, in contrast to the 1-phenylalkanols, $k_E > k_{EI}$.[8] This observation led to the mechanistic conclusion that the asymmetry of the starting alcohol was formally retained in an initially formed intermediate carbocation, the hydrophobic and hydrophilic sides of the alcohol precursor leading to segregation of the waters of solvation. The proposed asymmetric solvation of the prostaglandin-derived carbocation suggested that similar asymmetric carbocation solvation might be induced by carrying out the racemization of the 1-phenylalkanols in the presence of micelles. Interactions between the alcohol and micelle might lead, we hypothesized, to a microenvironment about the intermediate carbocation−water complex in which the hydrophobic core of the micelles would play the role of the hydrophobic chain of the prostaglandin: block solvent attack on the face opposite the departing water and lead to a similar decrease in k_{EI} relative to k_E. Here we report the effect of micellar SDS on the oxygen exchange reactions of **1** and **2**. The results of these kinetic studies are consistent with our predictions in that k_{EI} decreases for both **1** and **2**. The unexpected finding, however, is that micellar SDS also increases k_E for both alcohols, with the more hydrophobic **2** being more affected.

Material and Methods

Chemicals. (*R*)-**1** (99%), racemic **1** (98%), (*R*)- and (*S*)-**2** (≥99.6% ee), sodium dodecyl sulfate, SDS (98%), cetyltrimethyl ammonium bromide, CTAB, and D_2O (D, 99.8%) were obtained from Aldrich Chemical Co., Milwaukee, WI, and used as received. All solvents were analytical or HPLC grade and used without further purification. Tetrabutylammonium perchlorate, TBAP, was obtained from Fluka Chemika, Ronkonkoma, NY. Water, 97−99%-enriched in ^{18}O, was obtained from Isotec Inc., Miamisburg, OH. Deuterated dodecyl-d_{25} sodium sulfate (D, 98%) and *n*-hexane-d_{14} (D, 99%) were obtained from Cambridge Isotope Laboratories, Woburn, MA.

Unless described otherwise, all aqueous solutions of **1** and **2** were prepared by overnight sonication to ensure dissolution of the alcohols. (*R*)-and (*S*)-**1**, both 91%-enriched in ^{18}O, were prepared from the racemate and purified as previously described.[12] The ^{18}O enrichment is based on the relative intensities of the EI-MS parent peaks although the oxygen exchange reactions of both **1** and **2** were monitored using the more abundant mass spectral fragments resulting from the loss of the alkyl group (m/z = 107/109) which, for unknown reasons,[13] underestimates the ^{18}O content of the alkanols. These ion fragments indicated that the ^{18}O content of the labeled (*R*)- and (*S*)-**1** was 86%, significantly lower than that calculated from the parent ions. The bias in the oxygen composition data does not affect the qualitative conclusions of this paper and was incorporated into the kinetic analysis (below) to give accurate values for the rate constants of eqs 1−3.

Glassware. Kinetic studies were carried out in cone-shaped reaction vessels (Reactivials, Supelco, Inc., Bellefont, PA) washed with methanol and HPLC grade water and dried overnight in a 100 °C oven before use. Vial closures were Teflon-lined.

Racemization Kinetics of Nonenriched Alcohols. Samples were prepared from weighed portions of the (*R*)-enantiomers, SDS (for micellar samples), $NaClO_4$ (to adjust the ionic strength in one experiment), and HPLC grade water. In the case of **1**, the reaction vials were thermally equilibrated at 64.5 ± 0.1 °C prior to initiating the racemization reaction by the addition of concentrated acid (HCl or $HClO_4$). This procedure was modified for the studies of **2** to ensure that the acid concentration was identical in control and micellar samples. An aliquot of concentrated perchloric acid was added to a 10 mM stock solution of **2** at room temperature ($[H^+]$ = 0.105 M); a portion of this acidified alcohol solution was immediately transferred to a second vial containing a weighed amount of SDS. The kinetic experiment was initiated by simultaneous transfer of the control and micellar samples to a 64.4 ± 0.1 °C bath. Ten 100 μL aliquots were collected as a function of time for approximately 1 half-life of the racemization reaction for **2** and for 2 half-lives for **1**. Two additional samples were taken at 10−12 half-lives. These aliquots were removed, quenched with $NaHCO_3$, and extracted with hexane as previously described[12,13] except that the SDS-containing samples were stored at −75 °C overnight following addition of hexane and then brought to room temperature prior to transfer of the hexane extracts to clean vials. We found this cooling procedure necessary for efficient separation of the aqueous and organic layers in SDS-containing samples. The final hexane extracts were analyzed via HPLC for isomeric composition and GC−MS for isotopic composition.

Oxygen Exchange Kinetics of ^{18}O-Enriched (*R*)-1 in 0.1 M SDS. An aliquot of a hexane solution containing approximately 2.5 mg of 91%-^{18}O-enriched (*R*)-**1** was transferred to a 2 mL Reactivial, and most of the hexane (approximately 200 μL remained) was removed with a stream of dry nitrogen. A 2.00 mL aliquot of 0.100 M SDS in 0.0805 M HCl was transferred to the vial to give a solution approximately 10 mM in (*R*)-**1**; residual hexane was removed with nitrogen. The vial was sealed and mixed vigorously. The reaction was initiated by immediate transfer to a 65.0 ± 0.1 °C bath; ten 150 μL aliquots were taken, quenched, extracted, and analyzed for the isomeric and isotopic composition.

Concentration Dependence on SDS of Oxygen Exchange Reactions of 1. A 10 mM solution of 91%-^{18}O-enriched (*S*)-**1** in HPLC grade H_2O was prepared as described for ^{18}O-enriched (*R*)-**1** above except that the sample was sonicated overnight. Following addition of sufficient 4 M HCl to give 0.0960 M acid (found by titration of 50 μL aliquots of the final solution), the solution was mixed with a vortex mixer and cooled immediately in an ice bath. Aliquots (150 μL) of the chilled alcohol solution were added to vials containing weighed portions of SDS and sufficient sodium chloride to maintain a constant ionic strength of 0.20 M. Following vigorous mixing, the vials were simultaneously transferred to a 65.0 ± 0.1 °C bath. After 70 min (1 half-life), the vials were placed in an ice bath and 10 mg of $NaHCO_3$ was added to each to quench the reaction. Following vigorous mixing, the quenched samples were extracted with 600 μL portions of hexane; SDS samples were treated as described above. The hexane extracts were analyzed as described for the kinetic samples.

Comparison of the Effects of HCl and $HClO_4$ on the Oxygen Exchange Reactions of 2 in SDS. To portions of a 10 mM solution of (*R*)-**2** in 97%-^{18}O-enriched water, aliquots of either concentrated HCl or $HClO_4$ were added to give $[H^+]$ = 0.100 M. Two aliquots each of the acidified solutions were added to weighed portions of SDS; [SDS] = 0.100 M. Following vigorous mixing, these samples were

transferred to a 64.4 ± 0.1 °C bath and allowed to react for 150 min. The samples were placed on ice, quenched, extracted, and analyzed as described for the kinetic samples.

Isomeric and Isotopic Composition of Kinetic Samples. Chiral HPLC was used both to determine the isomeric composition for evaluating k_{rac} and to separate and collect each enatiomer as previously described[12,13] except that a hydrophobic column (3 cm × 4.6 mm, 3 μm C-18 Pecosphere, Perkin-Elmer, Norwalk, CT) was placed between the injection valve and the chiral analytical column to protect the latter from possible damage from residual SDS. The oxygen isotopic composition of the HPLC-isolated enantiomers and of the unfractionated hexane extracts of the kinetic samples was determined using GC-MS (electron impact) as previously described.[12,13] The relative proportions of ^{16}O and ^{18}O in the alcohols were calculated from the integrated intensities of the m/z = 107 and 109, respectively (the base peaks of both **1** and **2**, resulting from the loss of the alkyl group), selected ion chromatograms. The percentage of the unfractionated alcohol containing the predominant oxygen isotope of the solvent will be designated here as $\Sigma(O_{ex})$.

The combined HPLC and GC–MS data yielded the relative amounts of the four alcoholic species in each kinetic sample: **R**, **R′**, **S**, and **S′** (eqs 1–3). The time dependence of these four species and $\Sigma(O_{ex})$ allowed the evaluation of three experimental rate constants, k_{rac}, the rate constant for racemization, $k_{tot\,ex}$, the rate constant for exchange into the unresolved alcohol, and k'_{cross} (defined in ref 13), from which the microscopic rate constants k_{EI}, k_E, and k_I were obtained:

$$2(k_{EI} + k_I) = k_{rac} \quad (4)$$

$$(k_E + k_{EI}) = k_{tot\,ex} \quad (5)$$

$$(2k_I + k_E + k_{EI}) = k'_{cross} \quad (6)$$

Numerical values for the rate constants of eqs 4–6 for **1** were via obtained either (1) linear least squares methods or (2) the simultaneous nonlinear least squares fitting of all composition data.[13] The results were identical within experimental error. Equations 7–9, based on the previously reported kinetic analysis for the four equilibrating species of eqs 1–3,[13] describe the isotopic composition data for kinetic experiments using natural abundance alkanols in ^{18}O-enriched water (such as that for (*R*)-**2** here), expressed as percentages:

$$2\mathbf{R}_t = (1 - p)[(\mathbf{R} + \mathbf{S})_0][1 + \exp(-Bt)] + p[(\mathbf{R} - \mathbf{S})_0][\exp(-Ct) + \exp(-Dt)] \quad (7)$$

$$2\mathbf{S}_t = (1 - p)[(\mathbf{R} + \mathbf{S})_0][1 + \exp(-Bt)] - p[(\mathbf{R} - \mathbf{S})_0][\exp(-Ct) - \exp(-Dt)] \quad (8)$$

$$\Sigma(O_{ex}) = [(\mathbf{R}' + \mathbf{S}')]_t = p[(\mathbf{R} + \mathbf{S})_0][1 - \exp(-Bt)] \quad (9)$$

where $B = k_{tot\,ex}[H^+]$, $C = k'_{cross}[H^+]$, $D = k_{rac}[H^+]$, and p = the fraction of the aqueous solvent containing a different oxygen isotope than the starting alcohol. In eq 9 the term $p[(\mathbf{R} + \mathbf{S})_0]$ is equal to the absolute ^{18}O isotopic content of the solvent and should be reflected in the alcohol isolated at equilibrium, $(\Sigma(O_{ex}))_{eq}$. The oxygen isotopic composition based on the m/z = 107/109 ion fragments gives, however, erroneously low values for the ^{18}O content.[13] This experimental bias was incorporated into the nonlinear least squares analysis of the kinetic data for (*R*)-**2** as follows: The mean ^{18}O content of the equilibrium samples of unfractionated alcohol, **R**, and **S** was substituted as a constant $[(\Sigma(O_{ex}))_{eq,av}]$ for $p[(\mathbf{R} + \mathbf{S})_0]$ in eq 9:

$$\Sigma(O_{ex}) = [(\mathbf{R}' + \mathbf{S}')]_t = [(\Sigma(O_{ex}))_{eq,av}][1 - \exp(-Bt)] \quad (10)$$

Simultaneous nonlinear, nonweighted fitting of all **R**, **S**, and $\Sigma(O_{ex})$ (using MINSQ (MicroMath Scientific Software, Salt Lake City, UT) to eqs 7, 8, and 10 was then used to obtain optimal parameters for B, C, D, and p. The validity of this procedure was evaluated by comparison of the value of the parameter p found in the optimization with that based on the experimental value of $[\Sigma(O_{ex}))_{eq,av}]$. The optimized value of p in experiments 3 and 4 (Table 1, below) found via this fitting procedure agreed within 2% of the experimentally determined value, 0.901 ± 001 (optimization) vs 0.882 ± 0.005 (experimental); the precision is expressed as the standard deviation. Using eq 9 rather than eq 10 to fit the same data yielded values of p significantly higher (6–8%) than that from the equilibrium isotopic composition assays.

Surface Tension and Viscosity Measurements. The cmc of SDS in the presence and absence of 11 mM **1** at 25.0 ± 0.1 and 65.0 ± 0.1 °C was based on surface tension measurements made using a Fisher Scientific Surface Tensiomat 21; nine SDS concentrations were used for each cmc evaluation. The value of the cmc was the concentration at which the two straight lines in plots of surface tension versus concentration intersected. Viscosity measurements were made with Ostwald viscometers calibrated with aqueous solutions of sucrose.

Micellar SDS–Alkanol Association Constant Determination. The HPLC method of Arunyanart and Love[16] was used to determine the equilibrium association constants, K_{assoc}, of the alkanols with micellar SDS. The equilibrium constant, K_m, for interaction between monomeric SDS, SDS_m, and alkanols is related to the chromatographic retention behavior:

$$SDS_m + ROH \overset{K_m}{\rightleftharpoons} SDS_m{-}ROH \quad (11)$$

$$K_{assoc} = K_m N \quad (12)$$

where N is the aggregation number of SDS; in these experiments, we have used an aggregation number of 62[17] in calculating the values of K_{assoc}. The retention times, t_R, of 20 μL aliquots of 1 mM solutions of *rac*-**1** and (*R*)-**2** were monitored (λ = 254 nm) as a function of SDS concentration in the aqueous mobile phase using hydrophobic columns: 3 cm × 4.6 mm, 3 μm C18 or C8, Pecosphere (Perkin-Elmer, Norwalk, CT). The "column deadtime" t_o, was measured using an aqueous solution of $NaNO_3$ to calculate k', the chromatographic capacity factor: $k' = (t_R - t_o)/t_o$. The value of K_m was calculated from the ratios of slope to intercept of linear least squares fits of $1/k'$ as a function of $[SDS_m]$.

^{1}H NMR Measurements. The ^{1}H NMR spectra of 10 mM phenylalkanols in D_2O in the presence and absence of SDS were collected using a Bruker NR/200 FT NMR (4.7 T). T_1 determinations were done using standard inversion–recovery methods with 7–10 recovery times per determination.[18] The data were processed using Brucker software to obtain the integrated intensities. The intensities as a function of recovery times were fit to a three-parameter equation to extract the values of the initial and equilibrium intensities (I_{init} and I_{eq}, respectively) and the relaxation time T_1 using MINSQ; $I_\tau = I_{eq} - (I_{eq} - I_{init})\exp(-\tau/T_1)$. Chemical shifts were measured relative to an external standard of 0.5 M CH_3CN in D_2O.

Results

Correlation of Oxygen Exchange and Inversion. Parts a and b of Figure 1 show the enantiomeric oxygen exchange products of (*R*)-**1** and (*R*)-**2**, respectively, as a function of inversion in the presence and absence of SDS. The most striking feature of these figures is the SDS-induced increase in the rate of exchange with retention (**R16** in Figure 1a, **R18** in Figure 1b) for both (*R*)-**1** and (*R*)-**2**, with a larger effect seen for the latter compound. The data for (*R*)-**2** (Figure 1b) are most easily interpreted in that the starting material contained no ^{18}O; consequently, all of this isotope found in the alcohol originated from the solvent. In contrast, ^{18}O-enriched (*R*)-**1** starting material, while enantiomerically pure, contained considerable ^{16}O. Despite this complication, Figure 1 shows that SDS

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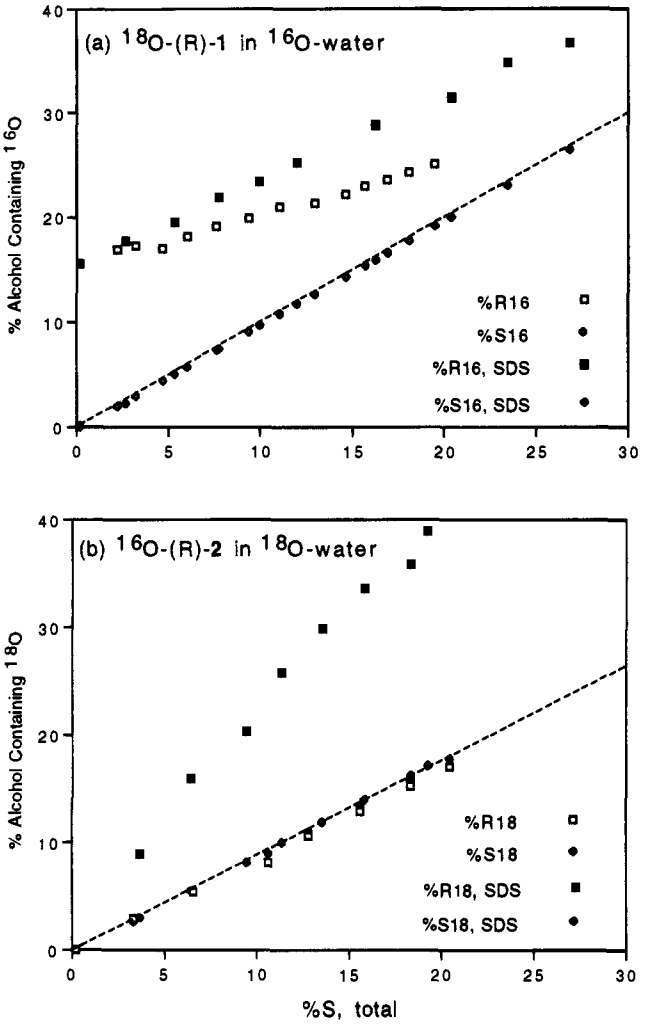

Figure 1. Oxygen exchange products formed in the acid-catalyzed racemization of (*R*)-**1** and (*R*)-**2** at 65.0 ± 0.1 °C as a function of the formation of the inverted isomer: (a) [^{18}O]-(*R*)-**1** in natural abundance water; (b) [^{16}O]-(*R*)-**2** in 95%-^{18}O-enriched water (Table 1). The open symbols represent the exchange products formed in the absence of SDS and the filled symbols those formed in the presence of 0.10 M SDS. The dotted lines represent the amount of inversion product expected if exchange occurred simultaneously with carbocation formation.

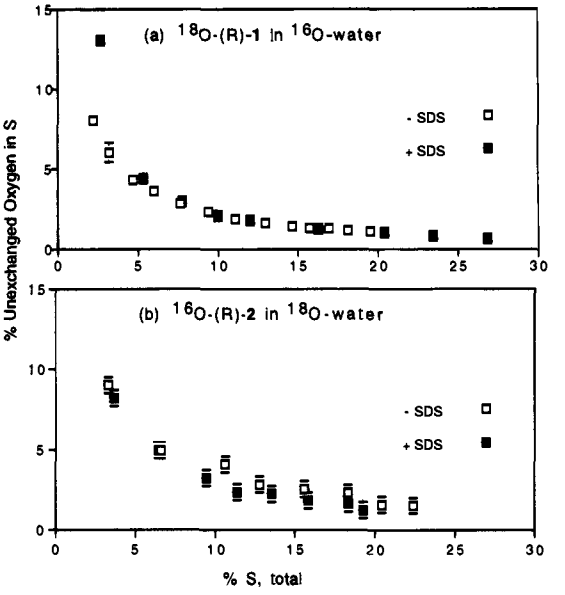

Figure 2. Percentage of unexchanged oxygen in the (*S*)-isomer formed in the acid-catalyzed racemization of (*R*)-**1** and (*R*)-**2** at 65.0 ± 0.1 °C as a function of the formation of the inverted isomer: (a) [^{18}O]-(*R*)-**1** in natural abundance water; (b) [^{16}O]-(*R*)-**2** in 95%-^{18}O-enriched water (Table 1). The open symbols represent the exchange products formed in the absence of SDS and the filled symbols those formed in the presence of 0.10 M SDS. The percentage of unexchanged oxygen is the difference in the percentage of the major oxygen isotope of the starting alcohol and that of the same isotope in the solvent. The latter was determined from mass spectral analysis of alcohol samples isolated at equilibrium (≥ 10 racemization half-lives). Error bars in (a) represent the standard deviation of replicate isomeric and isotopic composition assays; those in (b) represent the estimated error associated with the single or duplicate analyses of single samples.

increases oxygen exchange with the solvent without a change in configuration at the C1 chiral center for both **1** and **2**.

Parts a and b of Figure 2 contain profiles of the unexchanged oxygen in the inverted isomer as a function of inversion for (*R*)-**1** and (*R*)-**2**, respectively, in the presence and absence of SDS. The product, formed in 1−3% yield,[13] arises from backside attack of the initially formed carbocation by the departing water molecule. For both alcohols, the data points under the two experimental conditions essentially overlap. The small contribution of this internal return process is also seen in parts a and b of Figure 1 in which the amount of the exchange products formed with inversion (**S16** and **S18**, respectively) fall slightly below the dotted lines, representing simultaneous ionization and exchange.

Rate Constants. Table 1 contains a compilation of the rate constants determined in this study including those from the data of Figure 1 as well as those previously reported for **1** and **2**.[12,13] The lower values for all rate constants for [^{18}O]-(*R*)-**1** with no SDS in this table were attributed to either an acid concentration or temperature lower than in the other experiments for this alcohol.[13] Addition of 0.1 M SDS to the reaction medium reduces the rate constant for racemization, k_{rac}, by approximately 20% for **1** and more than 2-fold for **2**. The presence of SDS at a concentration of 1 mM (data not shown), below the cmc of 8.1 mM at 25 °C[17] and 6.1 mM at 65 °C (see below), however, had no significant effect on the rate of racemization of **1**. Experiments 1a and 1b were carried out at a constant ionic strength (μ) of 0.2 M by addition of $NaClO_4$ to experiment 1a, whereas the ionic strength of the media for experiments 2 and 3b (μ = 0.2 M) was higher than that of their nonmicellar controls [[^{18}O]-(*R*)-**1**, no SDS, and experiment 3b, respectively; μ = 0.1 M]. As previously reported,[12] a uniform increase of 30% in the absolute rate constants of **1** in media with μ = 2.0 M (HCl/NaCl) was interpreted as a neutral salt effect as the ratios of the oxygen exchange rate constants to k_{rac} were unaltered by high salt concentration. A similar nonspecific salt effect from added SDS would have, therefore, produced a modest increase in all rate constants for experiments 2 and 3b, rather than the observed decreases in k_{rac} and k_{El} simultaneous with increases in k_E.

As observed previously, about 1% styrene[12] and 3% 1-phenylbutene,[13] dehydration products from **1** and **2**, respectively, were detected by HPLC in the equilibrium samples (≥ 10 half-lives) for racemization carried out in the absence of SDS. In the presence of SDS, slightly larger amounts of these products were observed. Exact estimates of the amounts were not possible because of the overlap of the peaks from these species and UV-absorbing impurities in SDS; nonetheless, they constituted less than 1% of the starting alcohol at 1 half-life and less than 10% of the alcohol at equilibrium. Consequently, the elimination reactions were ignored in the kinetic analysis.

The rate constants for reactions in the micellar SDS (Table 1, calc) were calculated from the experimental rate constants and the fractions of **1** and **2** contained in the SDS pseudophase

Table 1. Rate Constants for Racemization and Oxygen Exchange Reactions of 1-Phenyl-1-ethanol (**1**) and 1-Phenyl-1-butanol (**2**) in Water and SDS Solutions[a]

		reaction conditions[c]			rate constants × 10^4, m^{-1} s^{-1}, 64.5 ± 0.5 °C				
expt	starting 1-PhROH[b]	[SDS], M	[alcohol], mM	f_{SDS}[d]	k_{rac}	$k_{tot\ ex}$	k'_{cross} or k_{cross}	k_E	k_{EI}
1a	[^{16}O]-(*R*)-**1**	0	4.6	0	15.5 ± 1.1				
ref 12	[^{16}O]**1** (N = 6) (*R*)- and (*S*)-**1**	0	20−44		16.0 ± 1.0	13.4 ± 1.1	13.9 ± 1.1	5.7 ± 0.9	7.8 ± 0.7
ref 13	[^{18}O]-(*R*)-**1**	0	14 (est)	0	13.8 ± 0.2	11.4 ± 0.1	11.7 ± 0.1	4.7 ± 0.2	6.7 ± 0.2
1b	[^{16}O]-(*R*)-**1**	0.100	5.1	0.66	12.0 ± 1.8				
2	[^{18}O]-(*R*)-**1**	0.100	11 (est)	0.66	11.9 ± 0.1	13.3 ± 0.1	13.5 ± 0.1	7.5 ± 0.2	5.8 ± 0.2
1-calc[e]	(*R*)-**1**	micellar SDS			10 ± 2				
2-calc[e]	(*R*)-**1**	micellar SDS			9.9 ± 1.0	13.3 ± 1.3	13.3 ± 1.3	8.3 ± 0.8	4.8 ± 0.5
3a[f]	[^{16}O]-(*R*)-**2**	0	10	0	11.9 ± 0.1	11.0 ± 0.1	11.5 ± 0.1	5.3 ± 0.2	5.7 ± 0.2
ref 13	[^{16}O]-(*R*)-**2** (N = 3)		10−13	0	11.8 ± 1.0	11.7 ± 0.6	11.6 ± 0.5	5.7 ± 0.1	5.9 ± 0.1
3b[f]	[^{16}O]-(*R*)-**2**	0.0989	10	0.89	4.39 ± 0.10	9.40 ± 0.03	9.62 ± 0.05	7.3 ± 0.1	2.1 ± 0.1
3-calc[e]	(*R*)-**2**	micellar SDS			3.5 ± 0.5	9.2 ± 1.5	9.4 ± 1.5	7.5 ± 1.2	1.7 ± 0.3

[a] Definitions of k'_{cross} and k_{cross} as well as the methods for obtaining the numerical values of k_{rac}, $k_{tot\ ex}$, and k'_{cross} (or k_{cross}) have been previously reported.[12,13] The precision of k_{rac}, $k_{tot\ ex}$, and k'_{cross} (or k_{cross}) is expressed as the standard deviation. Equations 4−6 were used to calculate k_{EI} and k_E. [b] Each entry represents a single kinetic experiment unless otherwise indicated; i.e., N = 6 for six experiments. [c] [SDS] = sodium dodecyl sulfate concentration in the medium. [H^+] = 0.10 M in all experiments; the exact acid concentration was known to 3−5% except for [^{18}O]-(*R*)-**1** with no SDS in which it was known only to ±10% although the relative values of the rate constants are accurate to three significant figures. $HClO_4$ was the acid source in experiments 1 and 3; HCl was used in experiment 2. Experiment 1a was done in 0.10 M $NaClO_4$. [d] f_{SDS} = fraction of alcohol present in the micellar pseudophase, calculated from K_{assoc} (Table 4). [e] The rate constants in micellar SDS were calculated from the experimental rate constants and f_{SDS} as shown in eq 13. For 1-calc, k_{rac} values from experiments 1a and 1b were used; for 2-calc, the numerical values used for k_{aq} were those for [^{16}O]**1**, N = 6; for 3-calc, the values from experiments 3a and 3b were used. [f] Experiments 3a and 3b were done with the same stock solution of (*R*)-**2** in 0.105 M $HClO_4$ in 95% ± 2%-^{18}O-enriched water.

Table 2. Rate Constants of Oxygen Exchange Reactions of 1-Phenyl-1-ethanol (**1**) and 1-Phenyl-1-butanol (**2**) Relative to Racemization in Water and SDS[a] at 64.5 ± 0.5 °C[b]

expt[c]	starting 1-PhROH	reaction conditions[d,e]	$k_{tot\ ex}/k_{rac}$	k_E/k_{rac}	k_{EI}/k_{rac}	$k_E/k_{tot\ ex}$
ref 12	**1**, N = 6 (*R*)- and (*S*)-**1**	$HClO_4$ or HCl	0.84 ± 0.05	0.36 ± 0.06	0.49 ± 0.05	0.43 ± 0.08
ref 13	[^{18}O]-(*R*)-**1**	$HClO_4$	0.83 ± 0.01	0.34 ± 0.03	0.49 ± 0.03	0.41 ± 0.02
2	[^{18}O]-(*R*)-**1**	HCl, 0.100 M SDS	1.10 ± 0.01	0.63 ± 0.01	0.49 ± 0.01	0.56 ± 0.02
2-calc[e]	(*R*)-**1**	micellar SDS	1.3 ± 0.2	0.84 ± 0.12	0.48 ± 0.07	0.62 ± 0.09
ref 13	[^{16}O]-(*R*)-**2**, N = 3	$HClO_4$	0.98 ± 0.10	0.48 ± 0.04	0.50 ± 0.04	0.48± 0.02
3a	[^{16}O-(*R*)-**2**	$HClO_4$	0.92 ± 0.01	0.45 ± 0.02	0.48 ± 0.02	0.48 ± 0.03
3b	[^{16}O]-(*R*)-**2**	$HClO_4$, 0.0989 M SDS	2.14 ± 0.05	1.67 ± 0.04	0.47 ± 0.03	0.78 ± 0.01
(3-calc[e])	(*R*)-**2**	micellar SDS	2.6 ± 0.4	2.1 ± 0.3	0.49 ± 0.08	0.82 ± 0.19

[a] SDS = sodium dodecyl sulfate. [b] The ratios were calculated from mean values of the rate constants compiled in Table 1. N is the number of kinetic experiments if more than one. [c] Experiment number, same as in Table 1. [d] Acid present at 0.10 M. [e] Micellar SDS; rate constants in micellar SDS calculated from the fraction of **1** and **2** present in the SDS pseudophase (Table 1) and the experimental rate constants.

(f_{SDS}). It is generally assumed that the observed rate constants for reactions occurring in SDS solutions are the weighted average of reactions occurring in the aqueous and micellar pseudophases:[19,20a]

$$k_{SDS(exp)} = f_{aq}k_{aq\ m} + f_{SDS}k_{micellar\ SDS} \qquad (13)$$

The values of f_{SDS} under the kinetic conditions were evaluated from the association constants, K_{assoc}, of micellar SDS with **1** and **2** (Table 4). For **1**, 66% of the alcohol is contained in the SDS pseudophase, whereas 89% of **2** reacts in this micellar phase. The large uncertainties in the rate constants in micellar SDS arise from large errors in K_{assoc} rather than from errors in the kinetic data.

Calculation of the rate constants in micellar SDS (calc, Table 1) using the partitioning model of eq 13 assumes that the micellar pseudophase is not altered by **1** and **2** themselves. To validate this assumption, we determined the cmc of SDS at 65 °C in the presence and absence of 10 mM *rac*-**1** and found the values to be identical within experimental error: 5.6 ± 0.3 and 6.1 ± 0.3 mM, respectively (data not shown). It appears, therefore, that the phenylalkanols do not significantly alter the cmc of SDS under the conditions of the kinetic studies. The smaller value of the cmc of SDS at 65 °C relative to that at 25 °C (8.1 mM[17]) is consistent with other reports that the cmc values of ionic micelles decrease with increasing temperature.[21,22]

Relative Rate Constants. The variation in values of the second-order rate constants in Table 1 reflects small differences in temperature and acid concentration as well as the effect of SDS. These differences cancel if the kinetic data are expressed as ratios since the three processes of eqs 1−3 arise via a common rate-determining step. Table 2 compiles the oxygen exchange rate constants relative to k_{rac}, the rate constant for racemization. Rapid equilibration of the carbocation with bulk solvent leads to equal probability of front and back side attack: $k_E/k_{rac} = k_{EI}/k_{rac} = 0.5$. Other values for these ratios indicate a more complicated reaction process. Values of $k_E/k_{rac} < 0.5$ for **1** and the corresponding 1-phenylpropanol, **3**, were interpreted

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as evidence of an ion−molecule pair in which the departing water blocked exchange with the bulk solvent on the front face of the initially formed carbocation.[12,13] Micellar SDS increases the importance of this exchange process with retention for **1** (k_E/k_{rac} = 0.84 ± 0.12) and even more for **2** (k_E/k_{rac} = 2.1 ± 0.3). For **2** in nonmicellar media, the values of k_E/k_{rac} are only slightly less than those expected if the carbocation rapidly equilibrated with the solvent (dotted line of Figure 1b). In contrast, the values of k_{EI}/k_{rac} for both alcohols obtained under all experimental conditions were only slightly less than 0.5; the slight deviation from this expected value reflects the small, but significant contribution of the internal return process (Figure 2). The SDS-enhanced exchange with retention is reflected in increased values of $k_{tot\,ex}/k_{rac}$: for **1**, 1.10 ± 0.01 (experiment 2) and, for **2**, 2.14 ± 0.05 (experiment 3b).

Comparison of HCl and $HClO_4$ as Acid Catalysts. Since the counterion often affects the kinetics and product distribution in reactions involving micellar catalysis or inhibition,[23] we compared the effect of HCl and $HClO_4$ on the oxygen exchange reactions of **2** in SDS. (*R*)-**2** in ^{18}O-labeled water containing 0.100 M SDS and either HCl or $HClO_4$ (0.100 M) were allowed to react under identical conditions for a fixed time. The racemization reaction proceeded at the same rate in both acids as judged by the identical values for the amount of the inversion product (*S*)-**2** formed (17.4%). Moreover, the percentages of **S16**, **S18**, **R16**, and **R18** obtained using either acid were identical within experimental error: for HCl, 2.54, 14.9, 43.1, and 39.5%, respectively; for $HClO_4$, 2.59, 14.8, 43.9, and 38.5%, respectively. These results, coupled with the lack of dependence of the oxygen exchange reactions of **1** in micellar media on the acid source,[12] lead to the conclusion that the differences observed in the exchange reactions of **1** and **2** with the solvent in 0.1 M SDS reflect only the influence of this additive.

Effect of SDS Concentration. Racemization of ^{18}O-enriched (*S*)-**1** in natural abundance water was allowed to proceed for a fixed time in the presence of varying concentrations of SDS. Table 3 shows that the extent of inversion (Σ(**R**) (%), HPLC) is inversely related to its fraction in the micellar pseudophase ($f_{micelle}$). The sample containing 9.3 mM SDS, a concentration near the cmc and equal to the concentration of the alcohol present, proceeded at a rate slightly slower than that of the sample with no additive. For the two samples containing SDS well above the cmc (102 and 199 mM SDS), the inversion reaction was inhibited considerably relative to the control, with the more concentrated SDS showing the largest inhibition.

On the basis of the extent of inversion (Σ(**R**) (%), Table 3), the percentages of the exchange products (**R16** and **S16**) expected were calculated using the rate constants for **1** in aqueous solution ([^{18}O]-(*R*)-**1**, Table 1). The experimental and calculated values for the exchange products formed from [^{18}O]-(*S*)-**1** with no additives (none) are in excellent agreement: **S16** = 25.0% (exp) vs 24.8% (calc) and **R16** = 19.5% (exp) vs 19.3% (calc). The increasing differences between **S16**(exp) and **S16**(calc) with increasing [SDS] are, therefore, significant and show that the rate of exchange with retention (k_E) depends on $f_{micelle}$. The agreement between the experimental and calculated values for **R16** indicates that the partitioning between inversion with and without exchange (measured by k_{EI} and k_I, respectively) was not altered by SDS.

Effect of CTAB. Table 3 also shows that the cationic micelle cetyltrimethylammonium bromide (CTAB) inhibited the inversion reaction. In contrast, CTAB had no effect on either oxygen exchange process (exp = calc) even though a significant portion of **1** appears to be in the CTAB pseudophase ($f_{micelle}$ = 0.2). Nonmicellar anionic tetrabutylammonium perchlorate (TBAP) altered none of the reactions.

Table 3. Oxygen Exchange Products formed in the Reactions of ^{18}O-enriched (*S*)-1-Phenyl-1-ethanol (**1**) in Natural Abundance Water as a Function of SDS Concentration and in the Presence of CTAB[a]

additive ($f_{micelle}$[b])	Σ(**R**), % (HPLC[c]) (exp)	**S16**,[d] % (% exchange with retention) [exp(calc[e])]	**R16**,[d] % (% exchange with inversion) [exp (calc[e])]
none (0)	19.6	25.0 (24.8)	19.5 (19.3)
9.3 mM SDS (0.07)[f]	19.1	25.4 (24.5)	18.9 (18.9)
102 mM SDS (0.66)	14.5	26.7 (22.1)	14.3 (14.2)
199 mM SDS (0.76)	9.67	24.3 (19.8)	9.45 (9.40)
8.7 mM CTAB (0.2)[f]	17.6	23.6 (23.7)	17.3 (17.3)
9.4 mM TBAP (0)	19.5	24.8 (24.7)	19.2 (19.2)

[a] Samples of 10 mM 91%-^{18}O-enriched (*S*)-**1** in 0.096 M HCl and containing the additives indicated were allowed to react simultaneously for 70 min at 64.5 ± 0.1 °C. SDS = sodium dodecyl sulfate; TBAP = tetrabutylammonium perchlorate; CTAB = cetyltrimethylammonium perchlorate. Numbers in bold-faced type are significantly different from the control (none) or from the calculated values. [b] $f_{micelle}$ = (moles of ROH in micelle)/(total moles of ROH) = K_{assoc} [SDS or CTAB monomer]/*N*. For SDS, K_{assoc} = 1.3 × 10^3 (Table 4), *N* = 62; for CTAB, K_{assoc} = 1.8 × 10^3 at 25 °C,[24] *N* = 61.[17] [c] The enantiomeric composition was determined by HPLC; since the starting material was (*S*)-**1**, the inverted isomer is (*R*)-**1**. [d] The data reported (exp) are the means of the replicate analyses. [e] The rate constants from Table 1 ([^{18}O]-(*R*)-**1**) were used to calculate the amount of each exchange product expected, **R16** and **S16**, on the basis of the percentage of inverted enantiomer, Σ(**R**), present in each sample. The ^{18}O enrichment of the starting material of this study was identical to that of experiment 2, Table 1, as the enantiomers were isolated from the same labeled racemic preparation. [f] The values for $f_{micelle}$ for these samples in which the alcohol was approximately equal to the monomeric surfactant should be regarded only as very rough estimates.

Table 4. Association Constants, K_{assoc}, between Micellar SDS and 1-Phenyl-1-ethanol (**1**) and 1-Phenyl-1-butanol (**2**) As Determined by HPLC

1-PhROH	$K_{assoc} \times 10^{-3}$	P_{mw}[b]	f_{SDS} in 0.100 M SDS
	A. At 25 °C		
1	1.2 (C18)		
	1.3 (C18)		
	1.3 (C8)		
mean	1.3 ± 0.1	(8.5 ± 0.7) × 10^1	0.66 ± 0.06
2	5.4 (C18)		
	6.5 (C18)		
	5.3 (C8)		
mean	5.7 + 0.7	(3.7 + 0.6) × 10^2	0.89 ± 0.15
	B. Temperature Variation (C18)		
1	1.5 (30 °C)	9.8 × 10^1	0.69
1	1.4 (40 °C)	9.2 × 10^1	0.67
1	1.3 (50 °C)	8.5 × 10^1	0.66
1	1.3 (65 °C)	8.5 × 10^1	0.66

[a] The values of the association constant per SDS monomer were determined by an HPLC method (ref 16) using eq 13 with the stationary phase shown in parentheses: C18 = octadecylsilyl; C8 = octasilyl. [b] P_{mw} = partition coefficient = $[ROH]_{SDS}/[ROH]_{aq}$ = $K_{assoc}[1/(SDS\ partial\ molal\ volume \times N)]$ = $K_{assoc}[1/(0.246\ L\ mol^{-1} \times 62)]$; SDS partial molal volume from ref 25. [c] f_{SDS} = (moles of ROH in SDS)/(total moles of ROH).

Binding of 1 and 2 to SDS. The values of K_{assoc} in Table 4 show that **2** binds more tightly to SDS than **1** by approximately a factor of 4 at 25 °C and that K_{assoc} for **1** is nearly invariant from 25 to 65 °C. Although large errors have been observed with the HPLC method used to obtain these data,[26] our value of K_{assoc} of SDS with **1**, 1.3 × 10^3, is similar to that reported for SDS with 2-phenylethanol, 1.7 × 10^3.[27] The larger error

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Table 5. ^{1}H NMR Longitudinal Relaxation Times, T_1, of Alkyl CH_3 Protons of 1-Phenyl-1-ethanol (**1**) and 1-Phenyl-1-butanol (**2**) in D_2O and 0.1 M SDS in D_2O[a-c]

1-PhROH	D_2O T_1, s	0.10 MSDS T_1, s	$T_1(D_2O)/T_1$(+SDS)
	a. 20.0 ± 0.5 °C		
(*R*)-**1**	1.37 ± 0.02	0.80 ± 0.03	1.7 ± 0.1
rac-**1**	1.36 ± 0.07	0.80 ± 0.02	1.7 ± 0.1
(*R*)-**2**	1.57 ± 0.09	0.92 ± 0.07	1.7 ± 0.2
	b. 64.0 ± 0.5 °C		
(*R*)-**1**	4.2 ± 0.3	2.5 ± 0.3	1.7 ± 0.2
rac-**1**	4.4 ± 0.3	2.7 ± 0.1	1.6 ± 0.1
(*R*)-**2**	4.6 ± 0.4	2.6 ± 0.1	1.8 ± 0.2

[a] SDS = sodium dodecyl sulfate. [b] The precision in T_1 is expressed as the standard deviation. [c] Measurements were made on samples of 11 mM (*R*)-**1**, 10.6 mM *rac*-**1**, and 9.89 mM (*R*)-**2**. For experiments with **1**, [SDS] = 0.11 M; for **2**, [SDS] = 0.12 M.

in K_{assoc} for **2** is inherent in the method in which the value is derived from the ratio of the slope to the intercept of a linear fit of $1/k'$ as a function of micellar SDS concentration; a stronger interaction results in a smaller intercept and, consequently, greater imprecision in larger values for K_{assoc}. The invariance of K_{assoc} of **1** with temperature is consistent with the pseudophase model in which no covalent bonds are broken or formed in the interaction of SDS with the alkanols in an entropy-driven process. We assumed a similar temperature invariance for K_{assoc} of **2** in calculating f_{SDS} for this alcohol under the kinetic conditions 64.4 ± 0.1 °C, Table 1.

^{1}H NMR. Table 5 contains ^{1}H NMR longitudinal relaxation times, T_1's, of the methyl protons of the alkyl chains of **1** and **2** in D_2O and in 0.1 M SDS-d_{25} in D_2O at 20 and 64 °C. The values of T_1 for both alcohols at both temperatures were smaller in the presence of SDS than in D_2O alone. Although the absolute values of the T_1's differed, the identical ratios of $T_1(D_2O)/T_1$(+SDS) for **1** and **2** at both temperatures suggest that micellar SDS produces similar alterations in the microenvironment of the alkyl methyl groups. T_1 is inversely related to τ_c, the molecular correlation time, which is, in turn, directly proportional to the viscosity surrounding the molecule or fragment.[18] If the decreased T_1 of the methyl protons of the alkanols in the presence of SDS relative to water reflects only alterations in bulk viscosity, η, the T_1 values should, therefore, be inversely related to the viscosity and the ratio $T_1(D_2O)/T_1$(+SDS) should equal the value of η_{SDS}/η_{water}. Our experimental value for η_{SDS}/η_{water} was 1.23 ± 0.03 (data not shown) at 65 °C, significantly smaller than $T_1(D_2O)/T_1$(+SDS) = 1.7 ± 0.01 (Table 5). This difference indicates that the microviscosity around the methyl residues in SDS exceeds that of the bulk solution in qualitative accord with a more constrained micellar environment. Menger and Jerkunica, using ^{13}C relaxation times, found that phenyl alkanoates solubilized in SDS experience a similar decrease in mobility, but that the fluidity of the medium was still substantially greater than expected for a solid hydrocarbon micellar core.[28] Unfortunately, the ^{1}H NMR signals from the methine protons of both **1** and **2**, expected to be better indicators of the overall motion of the alcohols, partially overlapped those of residual H_2O in the solvent so that accurate T_1 measurements could not be made for these protons.

No difference (±0.01 ppm) was observed in any of the ^{1}H chemical shifts of **1** and **2** in samples containing 0.1 M SDS relative to those dissolved in pure D_2O. The chemical shifts of the methyl protons of 10 mM solutions of **1** and **2** were 1.42 and 0.86 ppm, respectively, relative to CH_3CN (δ = 2.00 ppm) at 20 °C. The methyl protons of **1** in hexane (10 mM), on the other hand, appeared 0.34 ppm further downfield. Since approximately 70% of **1** is in the micellar pseudophase, 0.1 M SDS (Table 1), one would expect, if **1** statistically samples the bulk aqueous environment and a hydrocarbon-like environment in SDS, these methyl protons should appear approximately 0.23 ppm further downfield than in aqueous solution. The identities of the chemical shifts of these two alkanols in the presence of SDS and in pure water indicate, therefore, that the mean microscopic environment of these compounds in SDS solution closely resembles an aqueous one in terms of its polarity under the kinetic conditions of Table 1. Stark et al. similarly found no change in the ^{1}H NMR chemical shifts of phenyl acetate upon solubilization in SDS micelles and concluded that this material was located near the micelle surface.[29]

Discussion

Early kinetic studies of stabilized carbocations in micellar media revealed the general features of micellar effects on organic reactions.[20,30] In their classic studies of the fading of the triphenylmethyl carbocations in the presence of ionic micelles, Duynstee and Grunwald demonstrated that the reaction of the carbocations occurred at or near the micelle surface in the highly aqueous Stern layer.[31] Subsequent work has shown their results and conclusions to be predictive of other reactions occurring in micellar media. The differential effects of positively and negatively charged micelles on bimolecular, nonsolvolytic reactions can be ascribed to electrostatic interactions between the micelle and the reactant that either bring reactants together and, hence, speed the reaction or keep them apart and, consequently, slow the reaction. In contrast, micellar effects on unimolecular reactions involving carbocations, such as those of this study, are usually small and not as readily explained. These effects have been generally ascribed to reflect the reduced polarity of the micellar pseudophase and the reactivity of water in this reaction medium.[20e,30,31] Here, however, the observed effects of micellar SDS on the oxygen exchange reactions of **1** and **2** with the aqueous solvent can be most readily explained by micellar perturbation of the solvation sphere of the carbocation intermediates as shown schematically in Scheme 1. Such perturbations can account for the simultaneous SDS-induced enhancement of oxygen exchange with retention of configuration at C1 (k_E) and inhibition of oxygen exchange with inversion (k_{EI}) as well as the unaltered rate of inversion without exchange (k_I).

Solvation Sphere Perturbations. In their classic study of oxygen exchange with the solvent as a function of racemization of **1**, Grunwald et al.[3] suggested that the solvation sphere of the carbocation intermediate contained six water molecules, including the departing one. Scheme 1 shows such a solvated intermediate, **I**, and indicates the three competing processes (eqs 1−3) taking place at the chiral center to give the observed products. The five water molecules derived from the bulk solvent produce the two exchange products measured by k_E and k_{EI} ($k_{tot\ ex} = k_E$ and k_{EI}, eq 5). If one assumes that the values of

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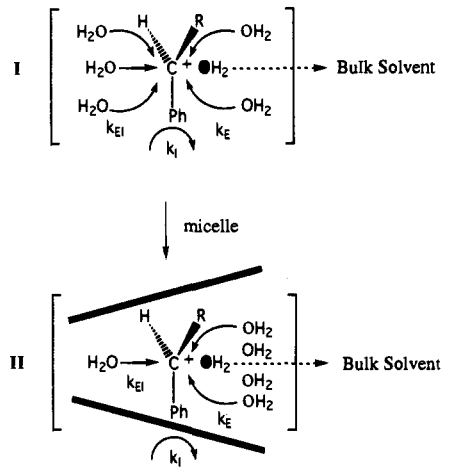
Scheme 1



the enantiomer-specific oxygen exchange rate constants measure the number of these five water molecules attacking opposite faces of the carbocation as shown, the ratio $k_E/k_{tot\,ex}$ (Table 2) can be used to give a heuristic description of the reactions of the carbocations derived from **1** and **2** in water and in an SDS medium. The experimental value of $k_E/k_{tot\,ex} \approx 0.42$ for **1** in the absence of micelles confirms Grunwald's earlier mechanistic conclusion that the departing water remains associated with the carbocation and, hence, blocks solvent attack on the front face of the carbocation. In contrast, the value of $k_E/k_{tot\,ex} \approx 0.5$ for **2** in aqueous solution shows rapid equilibration of the departing water with the bulk solvent (dotted arrow), resulting in equal probability of front- and backside attack. For **1** in micellar SDS ($k_E/k_{tot\,ex} = 0.62 \pm 0.09$), frontside exchange is favored with three water molecules near this side of the carbocation. The increased ratio of $k_E/k_{tot\,ex}$ for **2** in micellar SDS (0.82 ± 0.19) leads to even greater asymmetry so that four of the five water molecules can approach the same face as the departing water (**II** in Scheme 1). Models with different numbers of solvated water molecules lead to the same qualitative picture of a carbocation made formally asymmetric in micellar media by the ordering of the bulk solvent surrounding it; equilibration with the bulk solvent (dotted arrow) yields equal amounts of the two exchange products. The rate constant for the reaction of the carbocation from **1** with water in 50:50 THF/H_2O has been estimated to be 10^{11} s^{-1}, nearly diffusion controlled.[32] Consequently, the molecular events, occurring at the micelle interface and reflected in the enantiomer-specific rate constants of this study, occur on the picosecond time scale.

Whether the microscopic point of view focuses on the solvation of the carbocation itself or on that of the micelle surface, ratios of $\mathbf{k_E/k_{EI}} > 1$ require that the front face of the carbocation be exposed to more water molecules (or ones of higher reactivity) than the face opposite the departing water molecule. The mechanistic interpretation of our results (Scheme 1) in which SDS perturbs a fixed number of solvated water molecules is supported by the near invariance in $k_{tot\,ex}$ (Table 1) on addition of SDS to the reaction media for both **1** and **2**; the slight decrease in the value for this rate constant for **2** in micellar SDS reflects less rapid equilibration with the bulk solvent. Further support for the idea that the total number of water molecules in the immediate solvation sphere of the carbocation does not change in the presence of SDS comes from identical contributions of the internal return process (Figure 2) to the racemization of **1** and **2** in the presence and absence of SDS.

(32) Richard, J. P.; Jencks, W. P. *J. Am. Chem. Soc.* **1984**, *106*, 1373–1383.

The charged SDS head group may provide the perturbation to shift solvated water molecules from the back to the front face of the carbocation shown schematically in Scheme 1. This view focuses on the interaction between the negative charge on the anionic micelle with the waters of solvation rather than on the sulfate group with the carbocation itself. Bunton and Ljunggren suggested this latter interaction as the source of the smaller inhibition by SDS relative to that of CTAB in the S_N1 hydrolysis of sterically hindered arenesulfonates and aryl chlorides.[33] Attractive forces between the sulfate moiety and the hydrogens of the solvated water molecules would direct the nucleophilic oxygens toward the carbocation center, whereas the positively charged micelle CTAB would orient the waters of solvation in the opposite direction. This difference in orientation could account for our observation that CTAB inhibits the overall racemization of **1** but does not have the differential effects of SDS on oxygen exchange reactions (Table 3). Our comparative data are too limited to conclude that the observed increases in exchange with retention for **1** and **2** are specific to anionic SDS although the larger inhibition by CTAB of the overall racemization process is consistent with the observation that inhibition of S_N1 processes by cationic micelles is, in general, larger than that observed for reactions carried out in the presence of anionic micelles.[33,34]

Counterions other than Na^+ might be expected to alter the relative contributions of the two solvent exchange reactions in micellar SDS by interacting with the sulfate head group in such a way to attenuate its perturbation of the carbocation solvation sphere. Moss et al. found that the stereochemistry of 2-octanol formed in nitrous acid deamination reactions of micellarized optically active 2-aminooctane was dependent on the identity of the counterion.[23] They suggested that different counterions altered the contribution of a reaction occurring within an intermediate ion–molecule complex consisting of the 2-octyl carbocation, dinitrogen, and water relative to equilibration of this complex with the bulk solvent. These findings are similar to those of the present study in that micellar media increased the rate of a reaction at the same face of a carbocation as a departing neutral molecule: nitrogen in the case of the deamination reaction and water in the racemization of **1** and **2**. The reports differ significantly, however, in that the reactants in the deamination reactions are the cationic micellar components, whereas **1** and **2** are not micellar themselves and have been studied here in anionic SDS rather than in a cationic micellar system. Furthermore, for reactions of **1** and **2** in the present study, SDS increases k_E, which measures a process involving the bulk solvent water molecules rather than a recombination of the components within the ion–molecule complex postulated in the deamination reactions. Despite these differences, Moss's results and interpretation that varying reaction conditions alter the organization of components within the ion–molecule intermediates support the suggestion that SDS may similarly reorganize the solvation sphere of the carbocations from **1** and **2**.

An alternative interpretation of the increase in k_E in the presence of SDS might focus on the binding of water and sodium counterions to the micelle surface to confer, in some way, increased reactivity to water in the vicinity of the carbocations. Micellar control of stereochemistry has been previously associated with tight binding of substrates at the micelle–water interface. Natrajan et al. have shown that borohydride reduction of the propellanedione carbonyls in an

(33) Bunton, C. A.; Ljunggren, S. *J. Chem Soc., Perkin Trans. 2*, **1984**, 355–361.

(34) Al-Lohedan, H.; Bunton, C. A.; Mhala, M. M. *J. Am. Chem. Soc.* **1982**, *104*, 6654–6660.

aqueous solution of CTAB is directed to one face of the dione substrate.[35] These authors suggest that the micellar binding of the substrate orients the reactive functionality so that borohydride concentrated at the micelle surface preferentially attacks only one face. In analogy to the propellanedione−borohydride reductions, SDS binding of **1** and **2** would generate carbocations with the side of the departing water molecule oriented toward bulk water molecules concentrated at the negatively charged micelle surface; such an intermediate is similar to **II** (Scheme 1). The tighter binding of **2** to SDS would lead to the observed increased importance of the exchange with retention process (increased k_E) for this alcohol relative to **1**. This focus on hydration of the micelle surface to confer preferential attack on one face of the carbocation does not so readily account for the near invariance of $k_{tot\,ex}$ ($k_E + k_{EI}$) for **1** and **2** as the model of Scheme 1 in which SDS simply shifts a constant number of solvated water molecules. This latter view predicts that other negatively charged micelles such as carboxylates would induce a similar partitioning of the oxygen exchange products formed from phenylalkanols. Studies are in progress to evaluate more completely the effect of CTAB and other micelles on the enantiomer-specific oxygen reactions of **1**, **2**, and other 1-phenylalkanols.

Other Interpretations. The small decreases in k_{rac} and k_{EI} for **1** and **2** in SDS media (Table 1) and by CTAB (Table 3) could be explained by reduced polarity of the reaction microenvironment; the effective dielectric constant at the surface of ionic micelles has been estimated to be approximately 30−40.[36-38] The stronger interaction between the more hydrophobic **2** and SDS, as measured by K_{assoc} (Table 2), is reflected in larger changes in all rate constants for this alcohol (Tables 1 and 3), and is consistent with the view that **2** resides more deeply than **1** in the hydrophobic core of the SDS micelle, away from the micelle−water interface. Al-Lohedan et al. reported a similar correlation between the degree of micellar inhibition and hydrophobicity in their studies of spontaneous anhydride hydrolysis.[34] The conclusion that the phenylalkanols occupy a water-deficient environment in the SDS pseudophase is, however, at odds with the ^{1}H NMR chemical shift data indicative of a highly aqueous environment for **2**, as well as for **1**, in the presence of SDS. This aqueous microscopic environment in micellar SDS is one in which methyl protons at (for **1**) or near (for **2**) the chiral center have reduced mobility (smaller T_1's). Most importantly, the observed increases in the rate constant k_E in the presence of SDS (Tables 1 and 2) are not compatible with water-deficient microenvironments about the intermediate carbocations. The porous, water-permeated micellar SDS environment around **1** and **2** indicated by our ^{1}H NMR chemical shift data is compatible with the current view of micelles as water-permeated structures;[39] only the degree to which water molecules penetrate the hydrocarbon core and how this interaction is described remain controversial.[40]

The slight increase in elimination products from **1** and **2** in the presence of SDS is compatible with a reaction medium of reduced polarity. Although we cannot rule out the possibility that some oxygen exchange products arise from addition of water to styrene and phenylbutene, it is unlikely that these reactions slow relative to racemization, would be stereospecific. Grunwald et al. estimated the rates of the dehydration of **1** and hydration of styrene to be 0.03% and 3%, respectively, of those for racemization of **1** at 54.3 °C.[3]

Nucleophilic participation of SDS itself in the frontside exchange process could lead to observed increases in k_E, but is, in our view, unlikely. The possibility of a double displacement mechanism involving SDS has been postulated by Sukenik and Bergman[41] to explain specific suppression of inversion by this surfactant in the solvolysis of the *p*-(trimethylammonio)benzenesulfonate of 2-octanol. This mechanism requires that micellar SDS has nucleophilic properties unusual for an alkyl sulfate. While nucleophilic participation of SDS in the oxygen exchange reactions of both **1** and **2** cannot be excluded, the identity of the ^{1}H NMR chemical shifts in water and in SDS media provide no evidence of a water-deficient SDS environment about the phenylalkanols necessary to confer, as suggested by Sukenik and Bergman, an uncharacteristically high nucleophilicity to SDS. Furthermore, Okamoto et al.[42] found that both SDS and the more nucleophilic CTAB inhibited to a similar degree the hydrolysis of chiral 1-methylheptyl trifluoromethanesulfonate and changed the stereochemistry from net inversion (70%) in a nonmicellar medium to net retention, with CTAB causing the larger change.

Summary and Conclusions. We have shown that micellar SDS is selective in its effect on the three competing processes in the change of configuration at the chiral carbon in two secondary alcohols in aqueous media: Micellar SDS decreases substitution (O exchange) with inversion, enhances substitution (O exchange) with retention, and does not alter inversion without substitution. These differential effects can be accounted for by a mechanism in which the anionic micelle perturbs only the arrangement, but not the number, of water molecules within the solvation sphere of the intermediate carbocation.

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