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Binary mixed micelles of chiral sodium undecenyl leucinate and achiral sodium undecenyl sulfate: I. Characterization and application as pseudostationary phases in micellar electrokinetic chromatography

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ABSTRACT

Sodium 10-undecenyl sulfate (SUS), sodium 10-undecenyl leucinate (SUL) and their five different mixed micelles at varied percent mole ratios were prepared. The critical micelle concentration (CMC), C_{20}, γ_{CMC}, partial specific volume, methylene group selectivity, mobilities and elution window were determined using a variety of analytical techniques. These surfactant systems were then evaluated as novel pseudostationary phases in micellar electrokinetic chromatography (MEKC). As a commonly used pseudostationary phase in MEKC, sodium dodecyl sulfate (SDS) was also evaluated. The CMC values of SUS and SUL were found to be 26 and 16 mM, respectively, whereas the CMC of mixed surfactants was found to be very similar to that of SUL. The C_{20} values decreased dramatically as the concentration of SUL is increased in the mixed micelle. An increase in SUL content gradually increased the methylene group selectivity making the binary mixed surfactants more hydrophobic. Linear solvation energy relationships (LSERs) and free energy of transfer studies were also applied to predict the selectivity differences between the surfactant systems. The cohesiveness and the hydrogen bond acidic character of the surfactant systems were found to have the most significant influence on selectivity and MEKC retention. The SUS and SDS showed the strongest while SUL showed the weakest hydrogen bond donating capacity. The basicity, interaction with n and π-electrons of the solute and dipolarity/polarizability were the least significant factors in LSER model for the surfactant systems studied. Free energies of transfer of selected functional groups in each surfactant systems were also calculated and found to be in good agreement with the LSER data.

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1. Introduction

Micellar electrokinetic chromatography (MEKC) is a separation technique that combines the powerful features of liquid chromatography and capillary electrophoresis [1,2]. In MEKC, neutral and charged solutes can be separated simultaneously based on their differential partitioning between the mobile phase and the pseudostationary phase. The mobile phase is an aqueous buffer, whose properties can be manipulated by addition of modifiers such as organic solvents, cyclodextrins, urea, chiral additives etc. The pseudostationary phase is usually a charged surfactant that is added to the mobile phase at concentration above its critical micelle concentration (CMC). One of the major advantages of MEKC over other common separation techniques is the viability of optimizing the selectivity by simply rinsing the separation capillary with a new separation buffer solution containing a desired surfactant. Sodium dodecyl sulfate (SDS), an anionic surfactant, has been widely used as a pseudostationary phase in many MEKC applications.

One of the successful approaches to modify the selectivity in MEKC has been the selection of a surfactant of different nature. To date, a number of new pseudostationary phases with diverse selectivities have been introduced as alternative to SDS [3,4]. Altering the counter ion of the surfactant [5–7], addition of organic solvents, urea and cyclodextrins [8–11] are found to be useful for selectivity modification of a given pseudostationary phase. Another effective approach to improve the selectivity in MEKC is the application of mixed micelles of two or more different surfactants [3,12]. The mixed surfactant systems can be especially advantageous when their constituents have diverse properties.

Selection of proper surfactant for separation of special chemicals with varied physicochemical properties requires an understanding of the nature of solute-micelle interaction. Linear solvation energy relationships (LSERs) model has been introduced as a powerful tool for the characterization of retention and selectivity of

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pseudostationary phases in MEKC [13–18]. Initially developed by Kamlet et al. [19,20], this model provides information about the physicochemical properties of the separation systems as well as the magnitude of the different interactions between the pseudostationary phases and the solutes. More recently, Platts et al. [21] showed improved accuracy of some of the solute descriptors with new symbols and modified the LSER model which can be written as

$$\log k = c + vV + eE + sS + aA + bB \tag{1}$$

where V, E, S, A, and B are known as Abraham solute descriptors and are correlated to the logarithmic retention factor ($\log k$). V and E are measures of a solute's McGowan's characteristic volume and the excess molar refraction, respectively. The solute dipolarity/polarizability is represented by the S term. The A and B terms represent the hydrogen bond acidity (donating ability) and the hydrogen bond basicity (accepting ability) of the solute, respectively. The system coefficients c, v, e, s, a, and b refer to differences in the aqueous buffer and the pseudostationary phases, between which the solute is transferring. The constant c represents the intercept and includes information about the ratio of pseudostationary and aqueous buffer phases. The v term is a measure of the relative ease of forming a cavity for the solute in the aqueous buffer and pseudostationary phase. It is also a measure of hydrophobic interaction and related to the cohesiveness and dispersive properties of the pseudostationary phase. The coefficient e depends on the difference in ability of the pseudostationary phase and the buffer phase to interact with n- or π-electrons of solute while the s coefficient measures the dipolarity/polarizibility difference between the two phases. The coefficients a and b are the hydrogen bond accepting and hydrogen bond donating strengths of the pseudostationary phase, respectively. Through a comparative study of the five coefficients v, e, s, a, and b for the eight pseudostationary phases, their chemical selectivities can be determined.

Some reports on mixed surfactant systems have been published using LSER to understand the influence of the surfactant composition in MEKC [3,22]. Fuguet et al. analyzed 55 single, mixed and modified surfactant systems reported in the literature from over 200 pseudostationary phases characterized by LSER [3]. Among these selected surfactant systems, lithium perfluorooctane sulfonate (LPFOS), a fluorosurfactant with a C8 chain saturated with fluorine atoms, was found to have the most different selectivity with the extremely negative a and high b coefficients that are not found in any other systems. Based on the attractive properties of LPFOS, any of the mixtures containing it as a cosurfactant may show a wide variation of selectivities. However, sodium salt of LPFOS is insoluble, thus it cannot be mixed with SDS or other sodium surfactants; it can only be mixed with lithium surfactants. The influence of mixed micellar systems of SDS-sodium deoxycholate (SDC) and SDS-sodium cholate (SC) on retention and selectivity in MEKC were examined by Khaledi et al. using LSER [22]. In a comparative study of the LSER coefficients in the individual and mixed micellar systems, it was concluded by the authors that hydrogen bonding interactions had a significant effect on selectivity of the pseudostationary phases in MEKC. The interactive properties of the mixed micelles were found to be different from the constituent individual micelles; however, the overall characteristics were found to be closer to one of the bile salt micelles in the mixture even at the equimolar compositions.

In the present work, monomers of sodium 10-undecenyl sulfate (SUS), an achiral surfactant, sodium 10-undecenyl leucinate (SUL), a chiral surfactant, and their five binary mixtures were prepared and studied systematically. Their CMC, C_{20} (surfactant concentration that reduces the surface tension by $20\,\mathrm{mN\,m^{-1}}$), γ_{CMC} (surface tension at CMC), partial specific volumes, methylene selectivity, mobilities, and the elution windows were determined using a variety of analytical techniques. They were then evaluated as pseudostationary phases in MEKC for separation of benzene derivatives with a wide range of chemical properties. As a commonly used pseudostationary phase in MEKC, SDS was also evaluated. To predict the selectivity differences between the eight surfactant systems, linear solvation energy relationships and free energy of transfer studies were conducted.

There are several objectives of this study. First, by changing the percent ratio of the two surfactants in their binary mixtures, the selectivity can be manipulated. Second, due to the protonation of carboxylate head group, amino acid-based chiral surfactants precipitate out of solution at acidic pHs, which limits their applications as pseudostationary phases. Their solubility can be significantly improved by combining them with highly soluble surfactants (e.g., SUS). The conformation and the charge density of the mixed micelles of SUL and SUS may vary at low and high pHs, which may affect the performance and selectivity of the mixed micelles. Lastly, the binary mixed micelles with carboxylate and sulfate head groups can be used as pH-responsive pseudostationary phases. McCarney et al. has recently used a pH-responsive polymer with sulfonate and carboxylate head groups, poly(sodium 2-(acrylamido)-2-methylpropanesulfonate)/11-(acrylamido)-undecanoic acid, (poly(NaAMPS/AmU)) [23]. At low pHs, the sulfonic acid groups in poly(NaAMPS/AmU) remain ionic whereas the carboxylate groups are not ionized. Both groups become ionized at higher pHs. Based on the static light scattering, quasi-elastic light scattering, viscometry, ^{1}H NMR spin–spin relaxation measurements, and fluorescence probe studies, it has been shown that the ionization of carboxylates changes the balance between ionic repulsion and hydrophobic interaction. As a result of this alteration, poly(NaAMPS/AmU) forms a compact conformation (unimer micelle) at acidic pHs and a more open configuration at basic pHs [24]. The change in conformation was found to affect the electrophoretic mobility, retention, selectivity, and separation efficiency. Higher electrophoretic mobility and greater affinity for majority of solutes were observed at lower pHs. In addition, very hydrophobic solutes with long alkyl chains were found to migrate with better efficiency at lower pHs.

These mixed micelles will be applied as chiral selectors for separation of chiral molecules at acidic and basic pHs and will be discussed in the subsequent parts of this series.

2. Experimental

2.1. Materials

All benzene derivatives, alkyl phenyl ketone homologues, N,N'-dicyclohexylcarbodiimide, L-leucine, chlorosulfonic acid, disodium hydrogenphosphate, sodium dihydrogenphosphate, and sodium hydroxide were obtained from Alfa Aesar (Ward Hill, MA, USA). N-hydroxysuccinimide and 10-undecen-1-ol were purchased from TCI America (Wellesley Hills, MA). Undecylenic acid and deionized water were obtained from Acros Organics (Morris Plains, NJ, USA), respectively and a water purification system from Millipore (Milford, MA, USA). All chemicals were used as received without further purification.

2.2. Preparation of sodium 10-undecenyl sulfate, 10-undecenyl L-leucinate and their binary mixtures

SUS and SUL were synthesized with minor modifications using procedures reported by Bergstrom and Lapidot, respectively, and reported elsewhere [25,26]. The following procedure was followed for preparation of the binary mixtures: 50 mM stock solutions of SUS and SUL were prepared separately. Given volumes of each