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Investigating hydrophilic and electrostatic properties of surfactants using retention on two mixed-mode liquid chromatographic columns



J. Hammer^{a,b,*}, J.J.-H. Haftka^a, P. Scherpenisse^a, J.L.M. Hermens^a, P. de Voogt^{b,c}

^a Institute for Risk Assessment Sciences, Utrecht University, P.O. Box 80177, 3508 TD Utrecht, The Netherlands

^b Institute for Biodiversity and Ecosystem Dynamics, University of Amsterdam, P.O. Box 94248, 1090 GE Amsterdam, The Netherlands

^c KWR Watercycle Research Institute, P.O. Box 1072, 3430 BB Nieuwegein, The Netherlands

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ABSTRACT

In environmental risk assessment, it is essential to understand the relationship between molecular structure and fate and toxicity of organic contaminants. For surfactants, physico-chemical parameters which can reflect the interactions that determine surfactant behavior are not well defined and are therefore needed for the development of robust quantitative structure-activity relationships (QSAR). For the present study, we have measured HPLC retention times of several hydrocarbon and perfluorocarbon surfactant groups on a mixed-mode weak anion-exchange (WAX) and mixed-mode hydrophilic interaction liquid chromatography (HILIC) stationary phase. The nonionic alcohol ethoxylates are well retained on the HILIC column. Retention of anionic surfactants on the HILIC column is likely influenced by the degree of hydration of the surfactants and electrostatic repulsion from silanol groups. Less hydrated anionic surfactants (perfluoroalkyl carboxylates, perfluoroalkyl sulfonates and alkyl sulfates) show minimal hydrophilic interaction while other better hydrated anionic surfactants (alkyl carboxylates and alkyl sulfonates) are well retained. The retention mechanism of surfactants on both columns seems to be related to their degree of hydration, albeit expressed in different retention behavior: generally, retention on the WAX phase increases when retention on the HILIC phase decreases, and vice versa. The retention times from both columns were used to calculate retention factors (k') and these were subsequently used in calculating parameters that reflect the electrostatic property (k_{AX}) and hydrophilic property (k_{HILIC}) that determine the interaction between the hydrophilic part of the surfactant and the stationary phase. In further development of predictive models, we suggest the use of k_{AX} for anionic surfactants and k_{HILIC} for nonionic surfactants.

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1. Introduction

Surfactants are high production volume chemicals with applications in industry and numerous consumer products. As a consequence of their widespread use and resulting emission, surfactants may enter the environment and can sometimes be detected in water [1], wildlife [2], and humans [3], and may exert physiological effects [4]. In the last decade, perfluorinated surfactants are of particular concern in the scientific community and for regulators because they have been recognized as being highly persistent [5], potentially bioaccumulative and toxic [6,7], and are often present in complex mixtures [8]. Prediction of the fate and potential effects

of surfactants in the environment is needed for regulation and requires an understanding of their environmental behavior.

The behavior of solutes in water is a result of the intermolecular forces between water-water and/ or water-solute molecules. For surfactants, these interactions can be divided into three physico-chemical properties: hydrophobicity of the alkyl chain, hydrophilicity of the head group structure, and for ionic surfactants the electrostatic character of the head group [9,10]. Hydrophobicity of organic compounds corresponds to a tendency of a chemical to escape the aqueous phase and is related to the energy that is needed for water to form a compound-surrounding cavity in the aqueous phase [9,11]. For surfactants, the hydrophobic property is mostly related to the length or size of the alkyl chain. The hydrophilic property of (ionic) surfactants originates from polarity, hydrogen-bonding ability, and charge density of the head group structure. Note that, compared to anionic surfactants, some non-ionic surfactants (i.e., alcohol ethoxylates) do not have such a

* Corresponding author at: Institute for Risk Assessment Sciences, Utrecht University, P.O. Box 80177, 3508 TD Utrecht, The Netherlands.
E-mail address: jorhammer@gmail.com (J. Hammer).

clear “head group” structure because their hydrophilic property originates from a chain of repeating polar ethoxylate groups. The hydrophilic property of these surfactants can therefore not directly be compared to that of the anionic surfactant head group structure, and for nonionic surfactants in the current study we therefore refer to the “hydrophilic part” of the surfactant rather than to the “head group”. Electrostatic interactions of the anionic surfactant head group can be responsible for specific sorption of ionic surfactants to other phases as well as the formation of ion-pairs or ion-bridges with other phases [12]. All these physico-chemical properties influence the arrangement of water molecules around the surfactant and determine whether a compound is well hydrated (kosmotropic) or poorly hydrated (chaotropic). The resulting hydration sphere of the surfactant has a major influence on the behavior of surfactants in water [13–17]. A relationship between hydration and retention of a compound on a stationary phase has been observed in hydrophilic interaction liquid chromatography (HILIC) and ion exchange chromatography [18–20]. The retention of surfactants on such phases therefore gives information about their physico-chemical properties and their behavior in water. Further quantification of these properties may result in usable parameters that can be applied in predictive models such as so-called quantitative structure-activity relationships (QSARs). These models are well developed for neutral chemicals [21,22], but are not applicable to ionized and/or surface active compounds. For the latter chemicals, parameters for QSAR models are currently not well defined [23,24]. The main focus of this work is the development of new parameters based on the retention on the HPLC columns that reflect different interactions of neutral and anionic surfactants. These parameters can be applied for understanding the interactions of surfactants with other phases and as descriptors in new models to predict their environmental fate and effects.

In a previous study, we used retention times from a C_{18} stationary phase in reversed-phase high-performance liquid chromatography (HPLC) as an alternative approach to determine hydrophobicity of nonionic and anionic surfactants [10]. The effect of hydrophobicity and chemical structure (carbon chain length) on retention on a HPLC column is well known. An example of such an effect for different classes of surfactants is given by Haefliger [25]. For the current study, we measured the retention and used the retention factors of nonionic and anionic surfactants from a mixed-mode Weak Anion Exchange (WAX) column to study and quantify the electrostatic property of the head group of anionic surfactants. Furthermore, retention of anionic and nonionic surfactants on a mixed-mode HILIC column was used to quantify their hydrophilic property. Additionally, the effect of pH and ionic strength on the retention of some surfactants on the HILIC column was studied. While some studies have used HILIC and WAX columns in combination with surfactants [26–28], these are mostly used for separation purposes rather than for understanding surfactant properties. We have tested a number of different surfactant classes including alcohol ethoxylates, alkyl benzene sulfonates, alkyl sulfates, alkyl sulfonates, alkyl carboxylates, perfluoroalkyl carboxylates, and perfluoroalkyl sulfonates. Within each class, homologues with different chain lengths were studied.

2. Experimental

2.1. Chemicals

In developing the parameters, single compounds were applied instead of complex technical mixtures. The limited number of compounds tested is sufficient to derive the parameters that we are interested in, and eventually these parameters may also be applied to technical surfactant mixtures. A similar approach was

used in an earlier publication where a parameter for hydrophobic interaction based on retention on a C_{18} column was derived [10]. An overview of all test analytes with chain lengths and number/positions of specific functional groups of individual compounds is given in Table 1. Sodium salts of alkyl carboxylates ($C_xCO_2^-$), perfluoroalkyl carboxylates ($PFC_xCO_2^-$) and perfluoroalkyl sulfonates ($PFC_xSO_3^-$), and alcohol ethoxylates (C_xEO_y) were obtained from Sigma-Aldrich (Zwijndrecht, The Netherlands). Sodium salts of linear alkyl benzene sulfonates ($C_xBzSO_3^-$) were synthesized by Johannes Tolls [29]. The compound $C_{13}EO_8$ was synthesized by Roy Sheppard, Unilever, Port Sunlight Research Laboratory [30]. Sodium salts of alkyl sulfates and alkyl sulfonates were obtained from Research Plus (Barnegat, NJ, USA). All organic compounds had purities higher than 98%. Ammonium acetate was purchased from Sigma-Aldrich. Methanol and acetonitrile were obtained from Biosolve (Valkenswaard, The Netherlands). Ultrapure water was obtained from a Millipore water purification system (resistivity $>18\text{ M}\Omega/\text{cm}$, Merck Chemicals, Amsterdam, The Netherlands).

2.2. Stationary phases

The Acclaim mixed-mode WAX column consists of $3\text{ }\mu\text{m}$ high-purity, porous, spherical silica particles with $120\text{ }\text{\AA}$ diameter pores ($50 \times 3\text{ mm} + \text{guard}$; Thermo Fisher Scientific, Amsterdam, The Netherlands), and promotes both hydrophobic and ion-exchange interactions. The functional group consists of a hydrocarbon alkyl chain of unknown length and a tertiary amine terminus and is proprietary bonded with the silica core [31]. The WAX column was used with a solvent-water mobile phase composition ranging from 80:20 to 100:0 (v/v) with 10 mM ammonium acetate at a temperature of 40°C with a flow rate of $0.2\text{ mL minute}^{-1}$. Similar to an earlier study with a C_{18} stationary phase, we used methanol as solvent in the mobile phase for the anion-exchange measurements. In the same study, it was observed that 5 mM ammonium acetate in the mobile phase helped shielding charges and reduced most of the electrostatic repulsion from silanol groups [10]. Thermo Fisher does not describe the composition of the HILIC and WAX column coatings in detail but to minimize strain on the MS detector and at the same time to reduce the electrostatic repulsion from silanol groups, 10 mM ammonium acetate was added to the mobile phase of both columns.

The Acclaim mixed-mode HILIC column ($50 \times 3\text{ mm} + \text{guard}$; Thermo Fisher Scientific) consists of $3\text{ }\mu\text{m}$ high-purity, porous, spherical silica particles with $120\text{ }\text{\AA}$ diameter pores. The functional groups consist of diols attached to a hydrocarbon alkyl chain of unknown length, which is subsequently bonded to the silica surface. The HILIC column therefore promotes both hydrophobic and hydrophilic interactions at different mobile phase compositions. Retention times of surfactants were measured at solvent-water compositions ranging from 40:60 to 98:2 (v/v) with 10 mM ammonium acetate. Acetonitrile was used as solvent because it resulted in much better separation and retention compared to methanol [32]. System setup, temperature and flow rate settings were identical to those used for the mixed-mode WAX runs.

Prior to each run, the columns were equilibrated with the mobile phase for at least 60 min. Both A and B channels that provided the aqueous and solvent mobile phase, respectively, contained equal concentrations of ammonium acetate (no precipitation was observed when dissolving ammonium acetate in methanol or acetonitrile). Surfactant mixtures that were injected contained a maximum of five compounds. The surfactant mixtures were prepared in a solvent mixture equivalent to the mobile phase composition of the respective run. An injection volume of $5\text{ }\mu\text{L}$ was used. Analyte concentrations ranged between 0.1 and 1 mg L^{-1} . Every retention time measurement was performed in triplicate and

Table 1
Overview of surfactants tested in the present study.

Surfactant type	Abbreviation	Chain length (x)	Functional groups (y)	pK _a ^a
Alcohol ethoxylates	C _x EO _y	10 12 13 14 16	4 4-8 4,8 4,8 4	n.a.
Alkyl benzene sulfonates	C _x BzSO ₃ ⁻	1, 8 - 10, 12, 13	n.a.	0.7 [27]
Alkyl sulfonates	C _x SO ₃ ⁻	5, 8, 10, 11, 13, 15	n.a.	-1.9 [28] ^b
Alkyl sulfates	C _x SO ₄ ⁻	8, 11, 13, 15, 16	n.a.	-3.6 [28] ^b
Alkyl carboxylates	C _x CO ₂ ⁻	2, 4, 9, 11, 13 - 16	n.a.	4.8 [27]
Perfluoroalkyl carboxylates	PFC _x CO ₂ ⁻	3 - 7, 9, 11, 12	n.a.	-0.5 [29] ^b
Perfluoroalkyl sulfonates	PFC _x SO ₃ ⁻	4, 6, 8	n.a.	-4.8 [30] ^b

n.a. = not applicable.

^a It must be noted that the pK_a values of the more acidic surfactants in this study (C_xSO₄⁻, C_xSO₃⁻ and the perfluorinated surfactants) are very difficult to determine experimentally [29,31,32] and while our references show discrete values they are mostly extrapolated or calculated by computer programs.

^b Approximations or calculated values.

because the variation did not exceed 0.01 min, the average of triplicate measurements was used for further calculation.

2.3. LC-MS/MS analysis

Nonionic and anionic surfactants were analyzed on a Perkin Elmer (Norwalk, CT, USA) liquid chromatographic system (PE series LC) coupled to a triple quadrupole mass spectrometer (SCIEX 3000 MS/MS system, Applied Biosystems, Nieuwerkerk aan den IJssel, The Netherlands) with a Turbo Ion spray source operated at 400 °C. Mass spectrometer settings of the analytes can be found in Hammer et al. [10]. Chromatograms were integrated with Analyst 1.4.2 (Applied Biosystems).

3. Results and discussion

3.1. Retention of anionic surfactants on the mixed-mode WAX column

On the WAX column, anionic test analytes are retained by hydrophobic interactions with the alkyl chain as well as by electrostatic attraction with the anion-exchange functionality [28,31]. On silica-based columns retention of anionic compounds can also be affected by electrostatic repulsion originating from silanol groups that are negatively charged at pH 7 [33,34]. For the current study, it was attempted to minimize this effect by adding 10 mM ammonium acetate to the mobile phase (see Section 2.2). The relationship between the logarithmic retention factor and the methanol fraction in the mobile phase is considered linear for regular reversed-phase (C₁₈) columns [35–37] and can be expressed as:

$$\log k' = a \times \varphi + \log k'_0 \quad (1)$$

where the slope *a* represents the change in the logarithmic retention factor ($\log k'$) of the test analyte as a function of the methanol fraction (φ), and the intercept ($\log k'_0$) represents the logarithmic retention factor at φ_0 . The relationship between $\log k'$ and φ was observed to be linear for the test analytes measured with the mixed-mode WAX column (Fig. S1).

Within each surfactant group, the slope of the $\log k'$ versus φ relationship increased slightly (negatively) with increasing alkyl chain length of the homologues. This means that there is a fraction φ in the $\log k'$ versus φ relationship at which a surfactant with a longer alkyl chain length has the same $\log k'$ value as a surfactant with a shorter alkyl chain length. The point at which both relationships 'cross' each other can often be found by extrapolation and is called a convergence point [38]. For the hydrocarbon surfactant groups, the convergence point of the $\log k'$ vs φ plots was well above 100% methanol which resulted in a constant order of elution at all realistic (extrapolated) methanol fractions. However, the convergence point of perfluorinated surfactants was observed to be at $\varphi = 0.93$ (PFC_xCO₂⁻) and 0.95 (PFC_xSO₃⁻) (Figs. S1 E–F),

and at 100% methanol the longer perfluoroalkyl chains were less retained than shorter perfluoroalkyl chains (Fig. 1A). Jing et al. [39] showed that for PFC_xCO₂⁻ surfactants, the perfluoroalkyl chain has an electron-withdrawing effect on the carboxyl head group, reducing the charge-effect of the deprotonated oxygen atom. Using perfluorinated alcohols, Zygmunt et al. [40] further showed that the electron withdrawing effect is mostly a result from the perfluorinated carbon atoms that are closest to the head group. Therefore, an alkyl chain longer than a few perfluorinated carbon atoms should not further affect the charge-effect of the head group and the decrease in $\log k'_0$ with alkyl chain length for longer perfluorinated alkyl chains is more likely an effect of the shape or length of the alkyl chain and its interaction with the stationary phase. At high organic modifier concentrations, anion exchange columns can often exert HILIC separation mechanisms due to accumulation of water molecules around the charged functional group [19,41]. This may affect the ability of the perfluorinated surfactant to interact with the ion-exchange group. While the exact mechanism remains unclear, we can conclude that unlike for hydrocarbon surfactants the alkyl chain of perfluoroalkyl surfactants still affects the retention of these compounds at methanol fractions close to $\varphi = 1$.

The logarithmic retention factors from the $\log k'$ vs φ relationships were used in equation 1 to calculate logarithmic retention factors at 100% water ($\log k'_0$). A linear relationship between $\log k'_0$ and the number of carbon atoms in the alkyl chain was observed for all anionic surfactants. This is shown in Fig. 1B where the slope indicates the change in affinity of a surfactant in a pure aqueous mobile phase for the stationary phase per addition of a fluorocarbon or hydrocarbon unit to the carbon chain of the surfactant. Interestingly, the slope of perfluoroalkyl surfactants is comparable to that of hydrocarbon surfactants while, considering the highly hydrophobic nature of fluorocarbon moieties compared to hydrocarbons, one would expect the slopes of the perfluoroalkyl surfactants to be higher than those of the aliphatic surfactants [10].

3.2. Quantification of the electrostatic property of anionic surfactants

Because of the linear $\log k'_0$ vs C_x relationship, the effect of electrostatic interaction on retention was separated from the effect of hydrophobicity by extrapolating $\log k'_0$ to an alkyl chain length of zero carbon atoms ($\log k_{AX}$; Fig. 1B). The parameter $\log k_{AX}$ subsequently represents the interaction of the surfactant head group with only the anion-exchange functionality of the mixed-mode WAX column (Table 2). For an anionic compound to adsorb onto an ion-exchange site, it must first rearrange and remove a part of its hydration sphere in order to interact with the ion site [42,43]. Poorly hydrated ions have to remove less water molecules than strongly hydrated ions and therefore absorb more easily onto an ion-exchange site [44]. The ion-exchange retention of the anion can therefore be related to its degree of hydration which is usually

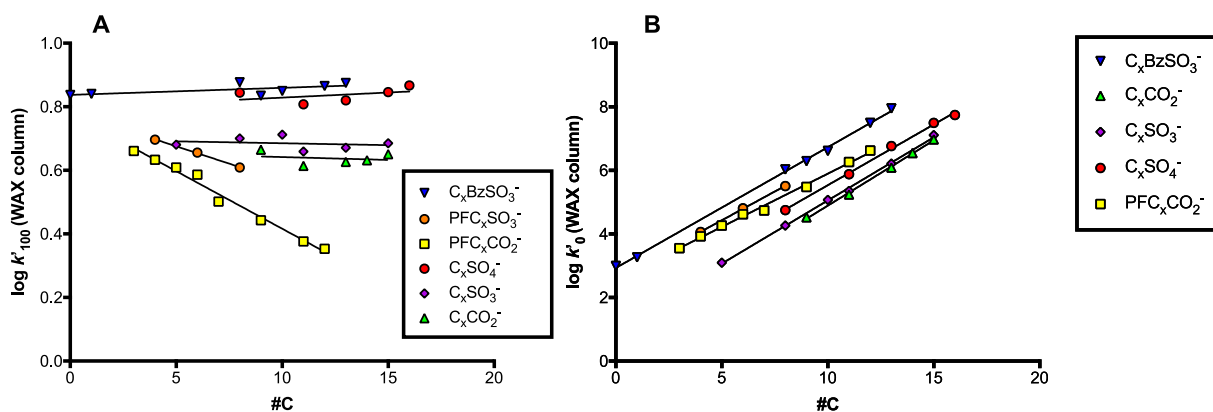


Fig. 1. Relationship between alkyl chain length of anionic surfactants and logarithmic retention factors on the WAX column, extrapolated to A) 100% methanol ($\log k'_{100}$) and B) 0% methanol ($\log k'_0$). All shown values are mean values of triplicates, variation in retention time between triplicates did not exceed 0.01 min.

Table 2

Head group structure of the surfactants used in the present study and measured $\log k_{AX}$ and $\log k_{HILIC}$ parameters for electrostatic and hydrophilic interactions.

Surfactant type	Head group structure	$\log k_{AX}$	$\log k_{HILIC}$
Alkyl carboxylates	CO_2^-	0.784	0.400
Alkyl sulfonates	SO_3^-	1.082	0.461
Alkyl benzene sulfonates	$BzSO_3^-$	2.932	0.149
Alkyl sulfates	SO_4^-	1.713	-0.179
Perfluoroalkyl carboxylates	$(PF)CO_2^-$	2.550	-0.091
Perfluoroalkyl sulfonates	$(PF)SO_3^-$	2.618	-0.642
Alcohol ethoxylates	EO_4	n.a.	0.137
	EO_5	n.a.	0.272
	EO_6	n.a.	0.431
	EO_7	n.a.	0.564
	EO_8	n.a.	0.620

n.a. = not analyzed.

a result of the charge-density around the ion [19,45]. Considering the current literature on hydration of anionic surfactants, it is difficult to find a quantitative measure for the degree of hydration because the accumulation of water molecules around the head group is often derived from the ability of the surfactant to ion-pair with specific counter ions [17,45,46] and simulations of the charge-density surrounding the head group [13,44,47]. Nevertheless, using such studies gives a general overview about whether some anionic surfactants are better hydrated than others. Shelley et al. [48] showed in computer simulations that alkyl carboxylates are well hydrated. They are therefore expected to have a relatively low ion-exchange retention which is reflected in the $\log k_{AX}$ value of $C_xCO_2^-$ (Table 2). Vlachy et al. [45] attempted to create a Hofmeister series for alkyl carboxylates, alkyl sulfonates and alkyl sulfates and determined alkyl carboxylates to be the best hydrated surfactants of the series while not much difference was found between alkyl sulfonates and alkyl sulfates. However, Yan et al. [17] later observed that due to a difference in hydration structure, alkyl sulfonates have a higher energy barrier for ion-pairing than alkyl sulfates and that alkyl sulfates therefore bind more easily to inorganic cations. Chen et al. [49] found similar differences in ion-pairing retention and observed alkyl sulfates to have stronger intermolecular interactions with cationic surfactants than alkyl sulfonates and related this to the difference in charge-density and hydration structure around the anionic surfactants [49]. This is in line with results from the current study where a higher k_{AX} value, and thus a higher ion-exchange retention, is observed for $C_xSO_4^-$ than for $C_xSO_3^-$. The head group of the perfluoroalkyl surfactants is affected by the perfluoroalkyl chain through its electron-withdrawing effect. This lowers the charge density of the head group and subsequently makes the $PFC_xCO_2^-$ head group less hydrated than that of $C_xCO_2^-$ [39,46].

The same goes for the $PFC_xSO_3^-$ surfactants when compared to $C_xSO_3^-$ [50]. Being less hydrated than the aliphatic surfactants with the same head group structure, these perfluorinated surfactants can more easily interact with the anion-exchange site on the WAX stationary phase. For the alkyl benzene sulfonates, the $\log k_{AX}$ value is relatively high in comparison to alkyl sulfonates. This is possibly related to the benzene ring that contributes to the retention due to the hydrophobicity of the aromatic ring, but cation- π interaction between the benzene ring and the tertiary amine group on the stationary phase may also positively affect retention [51]. To summarize, the degree of hydration of the surfactants may explain the difference in $\log k_{AX}$ between surfactant groups in Table 2.

3.3. Retention of nonionic and anionic surfactants on the mixed-mode HILIC column

The alkyl chain-diol combination of the HILIC column coating (see Section 2.2) results in the mixed-mode properties which are useful in the separation of hydrophobic compounds with different polarity. The hydrated diol groups on the HILIC column produce an immobilized layer of water at the surface of the HILIC column which is expected to promote retention through hydrophilic (polar and/or hydrogen-bonding) interactions with the surfactant molecule [52]. This retention mechanism is most present in a high organic modifier environment where water is mostly present in the immobile water layer (usually between 70–98% acetonitrile) [53]. At lower organic modifier concentrations, water will start to mix with acetonitrile and there is no incentive for the analyte to interact with the immobile water layer. Here, the hydrophobic alkyl chain on the stationary phase promotes retention through hydrophobic interaction with the carbon “tail” of the surfactant. In this way, the overall retention mechanism consists of a hydrophobic and a hydrophilic component.

Logarithmic retention factors ($\log k'$) of seven surfactant groups were measured with the mixed-mode HILIC column. The two retention mechanisms are reflected in Fig. 2A which shows that retention factors ($\log k'$) of surfactants decrease with increasing acetonitrile percentage due to a decrease in hydrophobic interaction. A minimum in $\log k'$ is reached at 70–80 % acetonitrile whereafter the retention increases again due to the hydrophilic interaction between the surfactants and the immobile water layer.

When focusing on the hydrophobic component of the retention mechanism in the mixed-mode HILIC column (i.e., retention measured at acetonitrile percentages below 70%), the nonionic alcohol ethoxylate $C_{13}EO_8$, which is more hydrophobic compared to anionic surfactants [10], showed higher $\log k'$ values compared to anionic surfactants of the same alkyl chain length (Fig. 2A). For

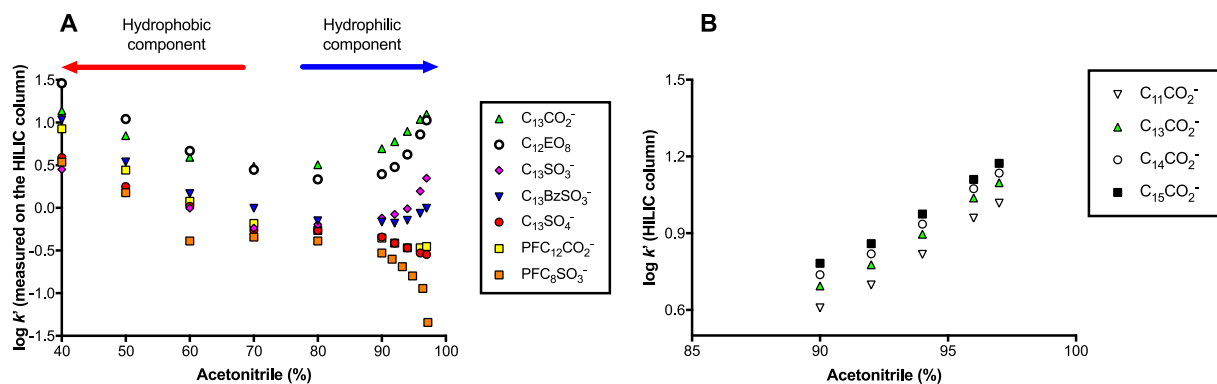


Fig. 2. A) Plot of logarithmic retention factors obtained with the mixed-mode HILIC column (10 mM ammonium acetate; pH 6.8) for one nonionic and six anionic surfactants with different head group structures versus percentage of acetonitrile in the mobile phase. The arrows indicate at which percentage range of acetonitrile in the mobile phase the hydrophobic or hydrophilic component dominates the retention mechanism. B) Logarithmic retention factors versus percentage of acetonitrile in the mobile phase for four alkyl carboxylates in the range that was used to determine k'_{HILIC} . All shown values are mean values of triplicates, variation in retention time between triplicates did not exceed 0.01 min.

the anionic surfactants with different head groups and nearly equal chain length, except for $PFC_8SO_3^-$, the order of elution was (starting with lowest $\log k'$ values): $C_{13}SO_4^- \approx C_{13}SO_3^- \approx PFC_8SO_3^- < PFC_{12}CO_2^- < C_{13}BzSO_3^- < C_{13}CO_2^-$. Perfluoroalkyl sulfonates longer than C_8 , and perfluoroalkyl carboxylates longer than C_{12} were not measured. This order of elution differs from expectations when retention would solely be a result of the hydrophobicity of these surfactants. Based on their expected hydrophobicity from Hammer et al. [10], perfluoroalkyl carboxylates should be most retained, followed by alkyl benzene sulfonates and alcohol ethoxylates and then the other anionic surfactants: alkyl carboxylates, alkyl sulfonates, and alkyl sulfates. This means that retention at low acetonitrile percentages on the mixed-mode HILIC column is likely influenced by another mechanism besides hydrophobicity. An overview of all surfactants measured with the mixed-mode HILIC column is shown in Fig. S2.

Silica-based stationary phases generally contain deprotonated residual silanol groups which have a negative charge at pH 7 and can contribute to retention through electrostatic interactions [10,33,54]. In the case of anionic surfactants, this results in electrostatic repulsion of anionic species. While the anionic surfactants in this study are usually fully ionized at pH 7, the addition of acetonitrile to the aqueous mobile phase lowers the dielectric constant of the mobile phase and this can result in an increase of the pK_a value of injected compounds (~ 0.3 log unit increase in pK_a value per 10% increase in acetonitrile) [55–58]. With their pK_a value now closer to the mobile phase pH, the effect of the ionized/nonionized fractions is more present. The elution order of surfactants at modifier strengths below 70% acetonitrile now makes more sense as alkyl carboxylates have a much higher pK_a and $\log k'$ value than the perfluoroalkyl carboxylates. The underlying effect of the repulsive electrostatic interactions of silanol groups is even more present at 60–80% acetonitrile, where hydrophobic and hydrophilic interactions are at a minimum (Fig. 2A). Here all the anionic surfactants elute roughly according to their pK_a value (Fig. S3). When the mobile phase acidity is lowered from pH of ~ 6.8 (resulting from the 10 mM ammonium acetate in the mobile phase [59]) to pH ~ 3.5 by replacing ammonium acetate with 10 mM of acetic acid, values of $\log k'$ for $PFC_{11}CO_2^-$ are at all acetonitrile percentages 0.4–1.0 log unit higher than $\log k'$ values at pH 6.8 (Fig. S4A). We expect $PFC_{11}CO_2^-$ to still be fully ionized at pH ~ 3.5 and this implies that the overall increase in $\log k'$ is probably an effect of the silanol groups that are now neutral as their pK_a value is around ~ 4.5 [33,34]. The electrostatic repulsion from silanol groups is then reduced. The alkyl carboxylates have a much higher pK_a value than perfluoroalkyl carboxylates and are completely protonated at a

mobile phase pH of 3.5. At this pH they are not affected by electrostatic repulsion and $\log k'$ values in the hydrophobic component range are, as expected, more than 2 times higher than at pH 6.8 (Fig. S4B). However, at pH 3.5, the contribution of the hydrophilic component to the retention of alkyl carboxylates seems to decrease and their lowest $\log k'$ values are subsequently found in the high acetonitrile percentage range ($\log k' = 0.17$ at pH 3.5 versus 1.0 at pH 6.8 in 98% acetonitrile). At first, it looks like an effect of the $C_xCO_2^-$ becoming protonated which may affect its interaction with the immobile water layer. However, the same trend is observed for the nonionic $C_{12}EO_8$ which also shows reduced $\log k'$ values at pH 3.5 and high acetonitrile percentages (Fig. S4C) which suggests that it is likely an effect of a change in the immobile water layer on the HILIC stationary phase. A more likely explanation might therefore be found in the silanol groups that are neutral at pH values below ~ 4.5 , which makes the stationary phase less polar and may reduce the ability of the mixed-mode HILIC material to retain a layer of water.

The addition of salts to the mobile phase can also affect the retention of analytes on the HILIC column through a salting-out effect or by suppressing electrostatic charges [11,60]. While the 10 mM ammonium acetate concentration used in the current study is probably not high enough to induce a salting-out effect it can reduce the effect of electrostatic interactions by suppressing charges on the stationary phase. This results in increased retention as electrostatic repulsion from the negatively charged silanol groups becomes less prominent. This effect may explain why $\log k'$ values for $C_{11}SO_3^-$, $C_{11}SO_4^-$, $C_{10}BzSO_3^-$ and $PFC_{10}CO_2^-$ decrease when the concentration of ammonium acetate is reduced to 5 mM (Fig. S5). Contrastingly, for $C_{11}CO_2^-$ an increase in $\log k'$ value is observed when reducing the ammonium acetate concentration (Fig. S5). An explanation might be found in their relatively high pK_a value compared to the other anionic surfactants (Table 1). According to Gilli et al. [61], the strength of hydrogen-bonding between two groups is stronger between compounds with small ΔpK_a . The pK_a value of $C_xCO_2^-$ is close to the pK_a value of acetate ($pK_a = 4.76$) [62], and may cause a preference for hydrogen-bonding between acetate and alkyl carboxylates over hydrogen bonding between water and alkyl carboxylates which results in less interaction between alkyl carboxylates and the immobile water layer. The remainder of the anionic surfactants in this study have very low pK_a values and are therefore not affected by this mechanism. However, it is difficult to deduce the exact mechanism from retention data obtained at only two concentrations of ammonium acetate and further research is needed to explain the effect of varying ammonium acetate concentrations on the retention of $C_xCO_2^-$.

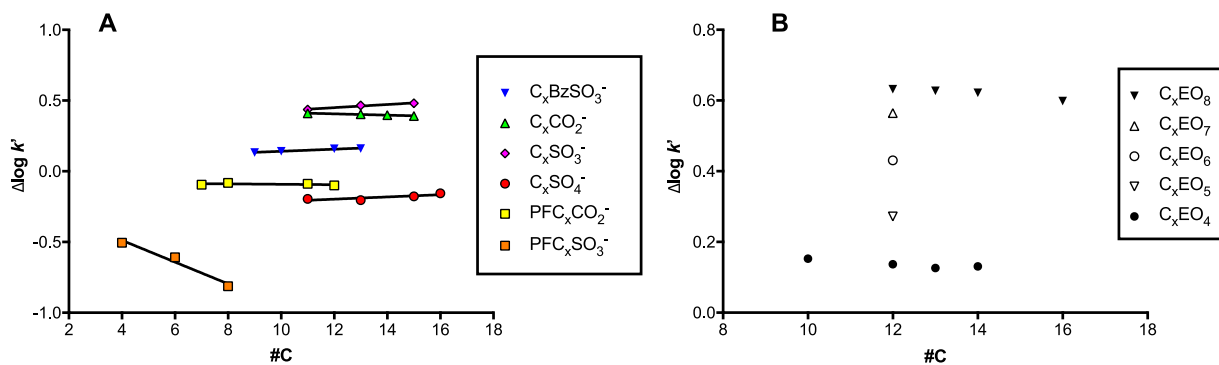


Fig. 3. Plots of $\Delta \log k_{HILIC}$ values for each surfactant versus alkyl chain length (#C) for A) anionic and B) nonionic surfactants. The $\Delta \log k_{HILIC}$ values express the decrease of increase in $\log k'$ between 90 and 97% acetonitrile in the mobile phase.

3.4. Hydrophilic interactions of anionic surfactants on the mixed-mode HILIC column

Hydrophilic interactions between surfactants and the immobile water layer on the HILIC column are most prominent between 90 and 97% acetonitrile, see Fig. 2A. From the seven surfactant groups that were tested, three ($PFC_xCO_2^-$, $PFC_xSO_3^-$ and $C_xSO_4^-$) showed no increase in $\log k'$ in this range and one of these compounds ($PFC_8SO_3^-$) even showed an extreme decrease in $\log k'$ (Figs. 2A and S2). Comparable trends were observed by Ibrahim et al. [19] while measuring retention of inorganic kosmotropic and chaotropic anions on a HILIC column. They concluded that poorly hydrated chaotropic anions partition predominantly into the organic phase because partitioning into the immobilized water layer works better for well hydrated anions. The more hydrated kosmotropic inorganic anions have a greater tendency to partition into the immobilized water layer which results in increased retention. In Section 3.2 we discussed the hydration of anionic surfactants based on literature sources and their $\log k_{AX}$ values from the current study and concluded that hydration of the surfactants can be ranked (from poor to well hydrated): $PFC_xSO_3^- \approx PFC_xCO_2^- < C_xSO_4^- < C_xSO_3^- < C_xCO_2^-$. The less hydrated $PFC_xSO_3^-$, $PFC_xCO_2^-$ and $C_xSO_4^-$ surfactant groups are barely retained above 80% acetonitrile in the HILIC column, while $C_xSO_3^-$ and $C_xCO_2^-$ are well retained. These trends are akin to the results presented in Ibrahim's paper [19] confirming the relationship between retention and hydration of the analytes on the HILIC column. While the degree of hydration of a compound affects the interaction of the analyte with the immobile water layer in the HILIC column, it also determines the effect of electrostatic repulsion. This was earlier discussed in Section 3.2 where we concluded that less hydrated compounds are most susceptible to electrostatic effects (see the decrease in $\log k'$ for $PFC_xSO_3^-$ with increasing solvent concentrations above 90% acetonitrile, Fig. 2A).

3.5. Quantification of the hydrophilic property of the nonionic and anionic surfactants

Retention factors that result from the retention on the HILIC column were used in an attempt to quantify the hydrophilic property of the surfactants for the purpose of future development of predictive models for surfactants behavior. When quantifying the hydrophilic property of the surfactants, focusing on the relative change in $\log k'$ ($\Delta \log k'$) in the hydrophilic component range between 90 and 97% acetonitrile is probably a better expression than comparing the highest $\log k'$ value between surfactants (see $C_{13}SO_3^-$ vs $C_{13}CO_2^-$ in Fig. 2A). The increase in $\log k'$ value ($\Delta \log k'$) in this range was therefore used to quantify the hydrophilic interactions with the mixed-mode HILIC column. Because $\Delta \log k'$ values are not dependent on alkyl chain length (Fig. 2B) and are

comparable for most surfactants within a surfactant group except for perfluoroalkyl sulfonates (Fig. 3A), the hydrophilic property was determined by the average $\Delta \log k'$ value per surfactant group which is subsequently expressed as $\log k_{HILIC}$. Values of $\log k_{HILIC}$ for each surfactant group can be found in Table 2. While the resulting values of $\log k_{HILIC}$ are arbitrary, we believe this is the most accurate approach in quantifying hydrophilic interactions with the mixed-mode HILIC stationary phase because it negates the influence of some background interactions that can influence retention.

Within the nonionic alcohol ethoxylates (C_xEO_y) surfactant group, a series of surfactants with alkyl chain lengths of C_{12} , C_{13} , C_{14} and C_{16} , and 4–8 units of ethoxylate moieties, were tested on the mixed-mode HILIC column. Alkyl chain length was found to barely affect $\log k_{HILIC}$ values while the addition of an ethoxylate (EO) group to the surfactant structure increased $\log k_{HILIC}$ with ~ 0.12 log units (Fig. 3B). This is expected as the EO unit contains an oxygen atom that is able to act as a hydrogen bond acceptor and is well hydrated [63]. Each addition of an EO unit will therefore further contribute to the hydrophilic interactions of the surfactant with the stationary phase (Table 2). However, while the overall value of $\log k_{HILIC}$ does increase, the increase in $\log k_{HILIC}$ per EO unit decreases with increasing number of EO units ($C_{12}EO_y$ in Fig. 3B).

4. Conclusion

Anionic surfactants that are more chaotropic, such as $PFC_xCO_2^-$, show increased retention on the mixed-mode WAX column compared with kosmotropic anionic surfactants such as $C_xCO_2^-$. This is probably an effect of the amount of water molecules in the hydration shell around the charged head group structure which can make it difficult for the surfactant to interact with the ion-exchange site. The opposite trend is observed for the hydrophilic retention of anionic surfactants on the mixed-mode HILIC column where $C_xCO_2^-$ and $C_xSO_3^-$ are well retained whereas $PFC_xCO_2^-$ and $PFC_xSO_3^-$ barely show retention. Retention on both columns is possibly driven by the hydration of the anionic surfactant head group which is directly related to the physico-chemical properties of the surfactants.

Retention factors from both columns were used to quantify the hydrophilic and electrostatic properties of the surfactant head group which resulted in the parameters $\log k_{HILIC}$ and $\log k_{AX}$, respectively. The resulting values of these parameters show that surfactant groups with a high $\log k_{HILIC}$ value usually have a low k_{AX} value, and vice versa. This again implies that the retention on both columns is probably a result of similar physico-chemical properties of the surfactant head groups. However, because of the very low retention of $PFC_xCO_2^-$, $PFC_xSO_3^-$ and $C_xSO_4^-$ on the HILIC column, we feel that $\log k_{AX}$ is a better representation of the physico-chemical properties of the head group that result in

the hydrophilic and electrostatic interactions of anionic surfactants than $\log k_{\text{HILIC}}$. On the other hand, the hydrophilic properties of the non-ionic surfactants C_xEO_y are well defined using the mixed-mode HILIC column and are best represented by their $\log k_{\text{HILIC}}$ values.

The chromatographic method used here may be transferred to other similar stationary phases as well considering that determined retention factors results into hydrophilic and electrostatic properties on a relative scale. The approach as described in this paper, opens new possibilities in the development of predictive models for ionic and surface active chemicals. This is an area with great interest, because until now the focus in this area is mainly on neutral compounds. Before going into applications, the insight into the retention of these more complex structures (the surfactants), as presented in this study, is needed. In a previously published paper a parameter for the hydrophobic property of surfactants ($\log k_{\text{C18}}$) was presented [10]. A logical next step is to use these three experimentally derived parameters as descriptors for molecular properties in the development of future QSAR models of surfactants.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:<https://doi.org/10.1016/j.chroma.2018.08.024>.

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