

Kinetic Medium Effects of Amphiphilic Cosolutes below Their Critical Micelle Concentration: The Effect of Sodium *n*-Alkyl Sulfates on the Neutral Hydrolysis of 1-Benzoyl-1,2,4-triazole

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Kinetic medium effects are presented for sodium *n*-alkyl sulfates (R = methyl to *n*-octyl) on the neutral hydrolysis of 1-benzoyl-1,2,4-triazole at 298.15 K in highly aqueous solutions below the critical micellar concentration. The observed rate-decreasing effects are quantitatively analyzed in terms of pairwise solute-solute interactions. It is shown that the effect of the alkyl chains cannot be accounted for on the basis of additivity of pairwise group interactions involving individual methylene moieties. Apparently, the sulfate group shields methylene moieties in close proximity for intermolecular interactions. Methylene groups, further away from the ionic functionality, are shielded less effectively. At the critical micellar concentration of the longer-chain sodium *n*-alkyl sulfates, the observed medium effects change dramatically as expected on the basis of the onset of micellization. No clear indication for pre-micellar aggregation was found. The medium effect of the sulfate moiety is estimated by extrapolation of kinetic medium effects to zero methylene groups and appears to be rate-retarding as well.

Introduction

Noncovalent interactions in aqueous media govern many important processes in biological, ecological, and chemical systems. Driving forces in supramolecular chemistry and molecular recognition processes are noncovalent by nature.¹ The complexity of large systems makes it difficult to obtain insight into the contributions of individual group interactions. These group interactions can be studied quantitatively by monitoring pairwise interactions between solutes in dilute aqueous solution. Kinetic medium effects of chemically inert cosolute molecules on the rates of organic reactions in dilute aqueous solutions directly reflect pairwise interactions between these cosolutes and both initial state and the activated complex.

Currently, considerable effort has been put into elucidating the nature of hydrophobic effects.² Recently, we have shown³ that a convenient way to probe the magnitude of hydrophobic interactions is offered by applying the additivity approach of pairwise group interactions, as brought forward by Savage and Wood⁴ (SWAG approach), in the analysis of kinetic solvent effects on organic reactions in dilute aqueous media. According to this approach, the effect of methylene moieties has been identified on rate constants of a series of organic reactions in dilute aqueous solution. In many organic reactions, the reacting species lose hydrophobic character during the activation process.

Hence, hydrophobic cosolutes and, particularly, the methylene groups stabilize the initial state to a greater extent than the activated complex and thus decrease the reaction rate constant.⁵ The extent to which these methylene groups retard the reaction reflects the hydrophobicity of these groups. Recognition of the gross assumptions underlying additivity schemes has led to impressive success in accounting for medium effects in dilute aqueous media-containing solutes, varying from monohydric alcohols,³ ureas,⁶ carboxamides,⁶ sulfonamides,⁶ sulfones,⁶ and sulfoxides⁶ to more complex cosolute molecules such as carbohydrates.⁷ In some cases, however, significant deviations from additivity have been identified.⁶

Herein, we describe medium effects of ionic cosolutes, *i.e.* a series of sodium *n*-alkyl sulfates (R = methyl to *n*-octyl) on the neutral hydrolysis of 1-benzoyl-1,2,4-triazole in dilute aqueous solutions. Further elongation of the hydrophobic moiety brings us into the field of anionic surfactants. Sodium *n*-dodecyl sulfate (SDS) is probably the best known representative of this class of compounds and one of the most frequently studied surfactants.⁸ Quantitative insight into the hydrophobic properties of these amphiphilic molecules will lead to a more detailed understanding of the behavior of these compounds in aqueous solution below and above the critical micelle concentration (CMC).⁸ Most interestingly, these studies will show how mutual interactions between constituent ionic and apolar groups in the alkyl sulfate determine the overall interaction process. In addition, the question is pertinent as to whether pre-micellar aggregates are formed

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(1) (a) Diederich, F. *Angew. Chem. Int. Ed.* 1988, 27, 362. (b) Vögtle, F. *Supramolecular Chemistry*; Wiley: Chichester, 1991. (c) Schneider, H.-J. *Angew. Chem. Int. Ed.* 1991, 30, 1417.

(2) (a) Privalov, P. L.; Gill, S. J. *Adv. Protein Chem.* 1988, 39, 191. (b) Muller, N. *Acc. Chem. Res.* 1990, 23, 23. (c) Wood, R. H.; Thompson, P. T. *Proc. Natl. Acad. Sci. USA* 1990, 87, 946. (d) Lee, B. *Polymers* 1991, 31, 993. (e) Blokzijl, W.; Engberts, J. B. F. N. *Angew. Chem. Int. Ed. Engl.*, in press.

(3) Blokzijl, W.; Engberts, J. B. F. N.; Blandamer, M. J. *J. Am. Chem. Soc.* 1990, 112, 1197.

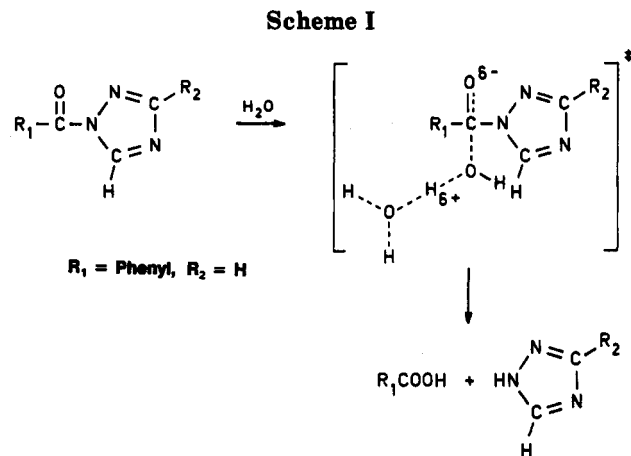
(4) Savage, J. J.; Wood, R. H. *J. Solution Chem.* 1976, 10, 733.

(5) Blandamer, M. J.; Burgess, J.; Engberts, J. B. F. N.; Sanchez, F. *Faraday Discuss. Chem. Soc.* 1988, 85, 1.

(6) Kerstholt, R. P. V.; Engberts, J. B. F. N.; Blandamer, M. J. *J. Chem. Soc. Perkin Trans. 2* 1993, 49.

(7) Galema, S. A.; Blandamer, M. J.; Engberts, J. B. F. N. *J. Am. Chem. Soc.* 1990, 112, 9665.

(8) See, for example, Brackman, J. C.; Engberts, J. B. F. N. *J. Colloid Interface Sci.* 1989, 132, 250.



below the CMC. In this study, we have mainly focused our attention on medium effects of the amphiphilic compounds below their CMC. Only for sodium *n*-heptyl and *n*-octyl sulfate were rate constants in micellar media determined.

A quantitative analysis of the observed medium effects of sodium *n*-alkyl sulfates enables us to monitor the effect of chain length and, subsequently, of the microenvironment in the vicinity of the ionic group below the CMC. Quantitative analysis of solute-solute interactions in terms of pairwise group interactions involving solutes with long alkyl chains evidently puts the SWAG approach⁴ to a severe test. Of particular interest is also the role of the polar sulfate group for the overall hydrophobicity of the compound. To our surprise, the sulfate group, when part of the sodium *n*-alkyl sulfate molecule, appears to retard our probe reaction to a similar extent as the methylene moieties do.

Results and Discussion

Previously,⁹ it has been shown that the dependence of rate constants of pH-independent hydrolysis reactions in dilute aqueous media on molality of added cosolutes (m_c) can be accounted for on the basis of eq 1.

$$\ln \left[\frac{k(m_c)}{k(m_c = 0)} \right] = \frac{2}{RT} \left[\frac{g_{xc} - g_{*c}}{m_0^2} \right] m_c - N\phi M_1 m_c \quad (1)$$

Herein, $k(m_c = 0)$ and $k(m_c)$ are, respectively, the rate constants in pure water and in the presence of added cosolutes. The right-hand-side term between brackets contains pairwise Gibbs energy interaction parameters representing the difference in pairwise interactions of the cosolute molecule(s) with the reactants (c) and activated complex (*). In eq 1 m_0 is the standard state, 1 mol kg⁻¹. Henceforth, the term between brackets is referred to as G(C). The second term in the right side of the equation accounts for the changing reactivity of water with increasing cosolute concentration. The practical osmotic coefficient of water is given by ϕ and the integer N is a mechanism-related parameter, representing the number of water molecules involved in the activation process. For dilute solutions, a satisfactory approximation sets ϕ equal to unity. M_1 is the molar mass of water. The neutral

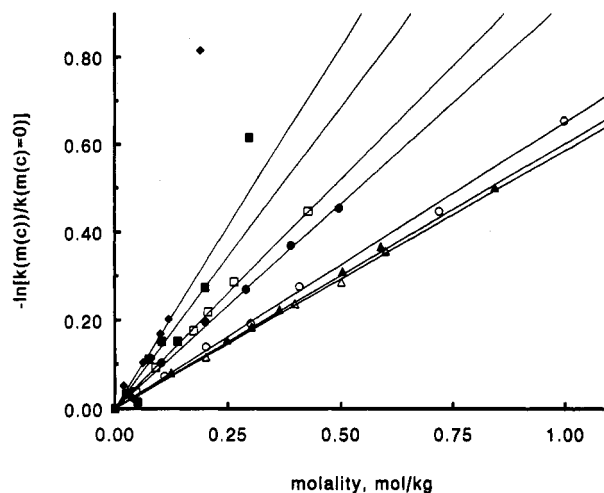


Figure 1. Medium effects on the pseudo-first-order rate constant for the hydrolysis of 1 at 25 °C, plotted as $-\ln[k(m_c)/k(m_c = 0)]$ versus the molality of sodium methyl sulfate, Δ ; sodium ethylsulfate, \blacktriangle ; sodium *n*-propyl sulfate, \circ ; sodium *n*-pentyl sulfate, \bullet ; sodium *n*-hexyl sulfate, \square ; sodium *n*-heptyl sulfate, \blacksquare ; and sodium *n*-octyl sulfate, \blacklozenge .

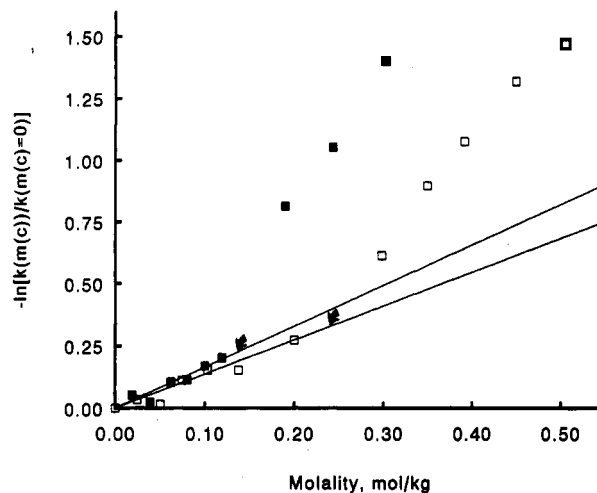


Figure 2. Medium effects of sodium *n*-heptyl sulfate (\square) and sodium *n*-octyl sulfate (\blacksquare) on the neutral hydrolysis of 1, at 25 °C, expressed as $-\ln[k(m_c)/k(m_c = 0)]$ versus molality. The arrows indicate the CMC.

hydrolysis of 1-benzoyl-1,2,4-triazole (1) occurs in the pH range of 3–5 and proceeds via a dipolar activated complex containing two water molecules (eq 1, $N = 2$) with three protons in flight¹⁰ (Scheme 1).

Medium effects on the neutral hydrolysis of 1, expressed as the dependence of $\ln[k(m_c)/k(m_c = 0)]$ on the molality of added sodium *n*-alkyl sulfates are shown in Figure 1. The concentration of added sodium *n*-alkyl sulfate was always smaller than 1 molal and all correlations, except for sodium *n*-heptyl and *n*-octyl sulfate, exhibit linearity ($r^2 > 0.999$) below the CMC. The correlation coefficients for sodium *n*-heptyl and *n*-octyl sulfate ($r^2 = 0.970$ and $r^2 = 0.956$, respectively) are significantly worse, which reflects the problems in determining accurate kinetic medium effects over a necessarily small concentration range below the CMC. As shown in more detail in Figure 2, the observed kinetic medium effects of sodium *n*-heptyl and *n*-octyl sulfate exhibit a clear break at the CMC. Apparently, the hydrolysis is retarded stronger by binding of 1 to the micellar surface than by pairwise interactions with the nonaggregated surfactants. All sodium *n*-alkyl

(9) Blokzijl, W.; Engberts, J. B. F. N.; Blandamer, M. J. *J. Phys. Chem.* 1987, 91, 6022.

(10) (a) Karzjin, W.; Engberts, J. B. F. N. *Tetrahedron Lett.* 1978, 1787. (b) Mooij, H. J.; Engberts, J. B. F. N.; Charton, M. *Recl. Trav. Chim. Pays-Bas* 1988, 107, 185.

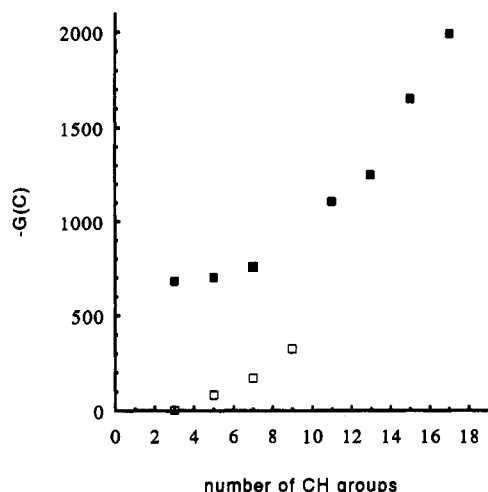


Figure 3. Medium effects of sodium *n*-alkyl sulfates (■) and *n*-alkanols (□) on the neutral hydrolysis of 1, at 25 °C. Plot of $-G(C)$ ($J\text{ kg mol}^{-2}$) versus the number of CH groups.

Table 1. Kinetic Medium Effects on the Neutral Hydrolysis of 1 in Aqueous Sodium *n*-Alkyl Sulfate Solutions at 25 °C. $G(C)$ and CMC^{11a} Values

alkyl group	CMC, mM	$G(C)$, $J\text{ kg mol}^{-2}$ ^a
methyl	—	-682 (7)
ethyl	—	-702 (7)
<i>n</i> -propyl	—	-762 (8)
<i>n</i> -butyl	—	not measured
<i>n</i> -pentyl	—	-1106 (13)
<i>n</i> -hexyl	520	-1249 (10)
<i>n</i> -heptyl	260	-1653 (45)
<i>n</i> -octyl	130	-1995 (100)

^a Errors are given within parentheses.

sulfates retard the hydrolysis of 1. Calculated values of $G(C)$ are listed in Table 1. In terms of the SWAG approach, $G(C)$ is composed of contributions of *n* methylene moieties in the alkyl chain, the ionic sulfate group, and the sodium ion, in formula $nG(\text{CH}_2) + G(\text{OSO}_3\text{-Na}^+)$. In the case of perfect additivity the increment between $G(C)$ values depends on the difference in the number of CH_2 groups only. In Figure 3, $G(C)$ is plotted as a function of the number of CH groups, which is equivalent to half the number of CH_2 groups. Obviously, the increment between $G(C)$ values of sodium *n*-alkyl sulfates increases with increasing chain length. The value of $G(\text{OSO}_3\text{-Na}^+)$ can be estimated by extrapolating the nonlinear relation to *n* is zero, assuming that the medium effect of the ionic part is not strongly dependent on the number of CH groups. This exercise provides $G(\text{OSO}_3\text{-Na}^+) = -660\text{ J kg mol}^{-2}$ which indicates an unexpected rate-decreasing effect. Although one could argue the validity of the assumption (*vide supra*), sodium *n*-alkyl sulfates induce a remarkably larger rate decreasing effect than linear alcohols with a similar number of CH groups.³ It is difficult to compare the value of $G(\text{OSO}_3\text{-Na}^+)$ with the medium effect of Na_2SO_4 , since in the pH range concerned the sulfate ion is partly protonated. Remarkably, in aqueous solutions of sodium sulfate (1 mol kg^{-1}) at pH = 3–5, the rate constant for the neutral hydrolysis of 1 is significantly enhanced. It must, however, be noted that a variety of other inorganic salts, such as NaI, retards the hydrolysis of 1 ($G(\text{NaI}) = -804 \pm 12\text{ J kg mol}^{-2}$).

As clearly shown in Figure 3, the medium effects of sodium *n*-alkyl sulfates on the hydrolysis of 1 cannot be analyzed using simple additivity procedures. The in-

creased CH contribution in longer-chain sulfates convincingly shows that the alkyl moieties become more hydrophobic as their distance to the sulfate group increases. Apparently, the sulfate group affects the availability of the methylene moieties for hydrophobic interactions. The effect may be partly steric in origin but also appears to involve mutual destructive overlap effects of the respective hydration shells. An extreme case is offered by the solvent effects of sodium methyl and ethyl sulfate, which are almost identical. Elongation of the alkyl chain of *n*-alkanols, used as cosolutes in the hydrolysis of 1 as well as of 1-benzoyl-3-phenyl-1,2,4-triazole, gave rise to a similar phenomenon.³ These observations can be explained by the fact that only remote alkyl groups are outside the region where the polar functional group can modify their kinetic medium effect. Studies of the clouding temperature of polymer solutions in the presence of sodium *n*-alkyl sulfates below their CMC did also show a strong dependence of the hydrophobic behavior of these amphiphiles on chain length.¹¹ These observations, however, seem to conflict with the results of an IR study to the hydration of sodium methyl to *n*-hexyl sulfonates¹² as well as with an NMR study of sodium sulfates in D_2O .¹³ These studies reveal that the differences in the number of water molecules in the hydration layer of these amphiphiles are merely dependent on the volume of the hydrophobic group and not so much on the actual distance to the ionic group.

The difference between the $G(C)$ values of sodium *n*-heptyl and *n*-octyl sulfate ($-340\text{ J kg mol}^{-2}$) can be taken as a measure for the "undisturbed" hydrophobicity of a methylene moiety in an alkyl chain. This value seems to be reached when the alkyl chain becomes longer than five to six carbon atoms. As shown convincingly by Abraham,¹⁴ coiling of alkyl chains in water is not very likely when the chain length does not exceed eight carbon atoms and therefore does not have to be taken into account in this study. In Figure 3, the $G(C)$ values of methanol, ethanol, *n*-propanol, and *n*-butanol are shown as well. Comparison shows that a sulfate group is slightly more effective than the hydroxy moiety in shielding the alkyl groups in the hydrocarbon chain. Remarkably, however, the absolute retardations brought about by the *n*-alkyl sulfates are larger than those by the linear alcohols. This phenomenon must be attributed to the rate-retarding effect of the sulfate moiety, as referred to earlier. The effects of inorganic salts on hydrophobic interactions will be discussed in a separate paper.¹⁵

Although experimental errors give rise to an unsatisfactory correlation coefficient, this seems to be caused by scattering of the data and not so much by curvature of the plots of $\ln[k(m_c)/k(m_c = 0)]$ versus the molality of sodium *n*-heptyl and *n*-octyl sulfate below the CMC. Since loss of linearity is associated with higher-order interactions, our results do not indicate the presence of pre-micellar aggregates.¹⁶ Aggregation does not seem to occur at a specific rate retardation for 1, expressed as $\ln[(k(m_c = \text{CMC})/k(m_c = 0))]$.

(11) (a) Schild, H. G.; Tirrel, D. A. *Langmuir* 1991, 7, 665. (b) Saito, S. *J. Polymer Sci. A-1* 1969, 7, 1789.

(12) Hecht, D.; Tadesse, L.; Walters, L. *J. Am. Chem. Soc.* 1992, 114, 4336.

(13) Clifford, J.; Pethica, B. A. *Trans. Faraday Soc.* 1964, 60, 1483.

(14) Abraham, M. H. *J. Chem. Soc., Faraday Trans. 1* 1984, 80, 153.

(15) Unpublished.

(16) Bonan, C.; Germani, R.; Ponti, P. P.; Savelli, G.; Cerichelli, G.; Bacaloglu, R.; Bunton, C. A. *J. Phys. Chem.* 1990, 94, 5331.

In conclusion, we have shown that the sulfate group affects the overall hydrophobicity of amphiphilic *n*-alkyl sulfates in such a way that it decreases the availability of methylene moieties for hydrophobic interactions, the effectiveness strongly depending on its actual distance to the methylene group. Using the SWAG formalism in a descriptive way, we have quantified the hydrophobic contribution to aqueous kinetic medium effects. Deviations of group additivity schemes were used, in retrospect, to elucidate the details of pairwise group interactions in dilute aqueous solutions. This approach has high potential in the study of the delicate balance between hydrophobic and hydrophilic interactions that determine solute-solute interactions in aqueous media.

Experimental Section

Materials. Demineralized water was distilled twice in an all-quartz distillation unit. All solutions were made up by weight and contained HCl (10^{-4} mol dm⁻³) to suppress catalysis by hydroxide ions. 1-Benzoyl-1,2,4-triazole was synthesized according to procedures described previously.^{10,17}

Sodium methyl and ethyl sulfate were prepared by hydrolysis of, respectively, dimethyl sulfate and diethyl sulfate in water and subsequent neutralization with NaOH according to a literature procedure.¹⁸ All other sodium *n*-alkyl sulfates were prepared from the corresponding *n*-alcohols and chlorosulfonic

acid in ether, using standard procedures as well.¹² The hydrogen sulfates were converted to their sodium salts with sodium carbonate and purified by continuous extraction with 2-propanol and recrystallization from this solvent. Only in case of sodium *n*-octyl sulfate, chloroform was used. The absence of Na₂SO₄ was checked by absence of precipitation of BaSO₄ on addition of BaCl₂ to a solution of the compounds in water.

Kinetic Measurements. Pseudo-first-order rate constants were determined by following the change in absorbance with a Perkin-Elmer λ2 UV/vis spectrophotometer, generally at 250 nm. Because of strong absorption of the cosolutes at 250 nm, the rate of hydrolysis of 1 in solutions containing sodium *n*-hexyl and *n*-octyl sulfate were measured at, respectively, 280 and 260 nm. About 3 μmol of a stock solution of 1 in acetonitrile (ca. 5×10^{-2} mol dm⁻³) was added to the reaction medium (1 mL) in a small volume quartz cell (0.3 cm width, pathlength 1 cm), placed in a thermostated cell compartment (25.0 °C ± 0.05 °C) of the spectrophotometer. The initial absorbance did not exceed 0.7 absorption units. The reaction was followed for at least 4 half-lives and excellent first-order kinetics was observed. Data were converted to reaction rate constants with a commercially available computer program. Reaction rate constants at each molality of cosolute were measured three times and were generally reproducible to within 0.7%. Each cosolute was measured at at least five molalities. In order to study pairwise interactions, measurements had to be performed below the CMC, to avoid contributions from aggregated clusters.

The pH of the solutions was 3.9–4.1 and was carefully checked before and after each measurement to avoid any possible effects of difference in protonation of the sulfate.

(17) Engbersen, J. F. J.; Engberts, J. B. F. N. *J. Am. Chem. Soc.* 1975, 97, 1563.

(18) Kurz, J. L. *J. Phys. Chem.* 1962, 66, 2239.