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Supramolecular Catalytic System Based on β−Cyclodextrin, Sodium Dodecyl Sulfate and Pralidoxime for the Hydrolysis of Paraoxon

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A set of physicochemical methods was used to study supramolecular interactions in an aqueous system based on the anionic surfactant SDS, oxime 2-PAM and macrocycle β-CD. The nature of the interactions between these components both in monomeric and aggregated forms was revealed. The kinetics of the reaction of paraoxon hydrolysis in the solutions was studied spectrophotometrically. It was found that the catalytic effect in this reaction increases in the aqueous medium if the supramolecular β-CD–SDS–2-PAM system is in the form of micellar aggregates.

Keywords: Cyclodextrin, surfactant, paraoxon, solubilization, self-aggregation, catalysis.

Супрамолекулярная каталитическая система на основе β−циклодекстрина, додецилсульфата натрия и пралидоксима для гидролиза параоксона

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Комплексом физико-химических методов были изучены супрамолекулярные взаимодействия в водной системе на основе анионного ПАВ ДСН, оксима 2-ПАМ и макроцикла β-ЦД. Была выявлена природа взаимодействий между компонентами данной системы, находящейся как в мономерном, так и в агрегированном виде. Спектрофотометрическим методом изучена кинетика реакции гидролиза параоксона в исследованных растворах. Установлено, что каталитический эффект в данной реакции увеличивается в водной среде, если система ДСН–2-ПАМ–β-ЦД находится в виде мицеллярных агрегатов.

Ключевые слова: Циклодекстрин, поверхностно-активное вещество, параоксон, солюбилизация, самоагрегация, катализ.

Introduction

In recent years, much attention has been paid to the development of new functional systems based on the supramolecular chemistry approach.[1] Within this approach, a key role is given to the design of macrocyclic scaffolds, which have a high selectivity for many organic reactions, in particular, hydrolysis of esters of phosphorus acids[2,3] being one of the ways to detoxify organophosphate neurotoxins and ecotoxicants.[4] Among supramolecular host macrocycles special attention is given to cyclodextrins that are particularly versatile building blocks for the design of materials for nerve agent sensors[5,6] and decontamination.[3,7] Such popularity is explained by the high affinity of the internal hydrophobic cavity of cyclodextrins to water-insoluble organophosphorus compounds.

A wide range of experimental studies have been also reported on the effectiveness of aggregate-forming surfactants with regards to hydrolytic reactions of phosphorus acid esters.[8-11] These aggregate systems are more efficient because they can more tightly bind substrates. Another approach to increase the effectiveness of the surfactant action against poisonings is to use oxime derivatives as surfactant functionalizing groups and counterions.[12-14] These oxime-based functionalized surfactants have high capability to neutralize organophosphorus-based compounds.

Thus, numerous papers are devoted to the hydrolytic cleavage of phosphonate nerve agents both in micellar core of surfactants and in hydrophobic cavity of cyclodextrins, while the catalytic activities of mixed cyclodextrin-surfactants systems towards dephosphorylation reaction have not been reported yet. The mixed cyclodextrin-surfactants systems combine the characteristics of composing species and also have many features compared to conventional single systems.[15] Therefore, in this paper we would like to construct the supramolecular systems based on β-cyclodextrin (β-CD) and ionic surfactant with oxime-counterion for effective hydrolysis of paraoxon (POX) being one of the most potent acetylcholinesterase-inhibiting pesticides. Since the cationic oxime pralidoxime (2-PAM) was taken as a surfactant counterion, the anionic sodium dodecyl sulfate (SDS) was chosen as a surfactant.

Experimental

Materials

SDS (99 %) and β-CD hydrate (99 %) were procured from Acros Organics. Pyridine-2-aldoxime methochloride (2-PAM chloride) (≥97 %) was purchased from Sigma-Aldrich. POX (99.1 %) was from ChemService. All the chemicals were used as received without further purification. 0.01 M PBS buffer (supporting electrolytes) and sample solutions were freshly prepared in deionized water (18.2 MΩ) obtained from a Millipore Direct-Q 5 UV water purification system.

Methods

Surface tension measurements were conducted on Du-Noüy tensiometer K6 with platinum ring (KRÜSS, Germany). The tensiometer was calibrated against deionized water. Platinum ring was thoroughly cleaned and dried before each measurement. The measurements were done in such a way that the vertically hung ring was dipped into the liquid to measure its surface tension. It was then pulled out from the solution carefully. Each experiment was repeated several times until good reproducibility was achieved. The results were accurate within ±0.1 $mN \cdot m^{-1}$.

NMR spectroscopy experiments were performed on an Avance-600 (Bruker, Germany) spectrometer equipped with a pulsed gradient unit capable of producing magnetic field pulse gradients in the *z* direction of about 56 $G \cdot cm^{-1}$.

The p*H* values of solutions were measured with a Hanna Instruments HI 9025 p*H* meter equipped with an HI 1330 glass membrane electrode.

The kinetics of the hydrolysis of POX were studied by spectrophotometry with an Analytik Jena Specord PLUS spectrophotometer by measuring the optical density at λ 400 nm (4-nitrophenoxide ion) under pseudofirst-order conditions. The observed rate constants (k_s) were calculated according to literature data.[16,17]

Results and Discussion

It is known that the formation of surfactant aggregates favours the catalytic action due to the effective encapsulation of the substrate, but the cyclodextrins have the ability to destroy surfactant aggregates because of high affinity of the alkyl chain of surfactant to the hydrophobic cavity of the macrocycle. To avoid the degradation of the SDS micelles in the presence of β-CD, we used 2-PAM as a counterion for the surfactant. In order to determine the concentration zones for the formation of mixed aggregates, the tensimetry method was used.

The aqueous solutions of β-CD–SDS–2-PAM with different equimolar concentration were studied by tensiometry (Figure 1). An increase in the proportion of components in the mixture leads to a decrease in the surface tension of the system at the water/air interface, and the course of change in surface tension reaches the plateau after a concentration equal to 5 mM. Consequently, starting with this concentration, micellar structures of β-CD–SDS–2-PAM are formed in the solution.

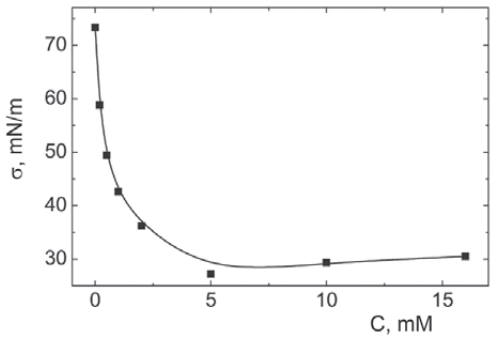

Figure 1. Concentration dependence of surface tension in the aqueous equimolar system of β-CD–SDS–2-PAM, 25 °C.

In order to verify the nature of the intermolecular interactions between the three components in supramolecular β-CD–SDS–2-PAM triad, ^{1}H NMR spectroscopy was involved. Initially, the interaction of the components in the monomeric state in an aqueous solution with

a concentration of 1 mM was studied (Figure 2). The ^{1}H NMR spectrum of the binary β-CD–2-PAM system shows no chemical shift of the proton signals of both components, which indicates that there is no interaction between β-CD and 2-PAM. In contrast, when SDS is added to the β-CD solution, the displacement of the signals of all macrocycle protons, except for H-1', occurs, which proves the assumption of the inclusive interaction of β-CD with SDS. The change in the signals of β-CD protons in the ternary β-CD–SDS–2-PAM system is probably due to the fact that 2-PAM molecules bind to one end of the SDS due to electrostatic attraction, which in turn probably affects the β-CD structure, the cavity of which binds the alkyl tails of SDS.

Next, the changes in the signals of SDS (Figure 3a) and 2-PAM (Figure 3b) protons were considered. A small shift (by 0.01–0.02 ppm) in both SDS and 2-PAM proton signals is seen in the ^{1}H NMR spectra of the binary SDS–2-PAM system, indicating the interaction between them. When the β-CD macrocycle is added to SDS–2-PAM system, methyl SDS protons undergo the largest displacement (by 0.05 ppm), confirming the interaction of SDS–2-PAM complex with the macrocycle due to hydrophobic association between the alkyl tail of SDS and the internal cavity of β-CD. The addition of β-CD does not affect the positions of 2-PAM proton signals, indicating that there is no effect of β-CD on the oxime molecule bound to the surfactant molecule. Thus, the study of intermolecular interactions

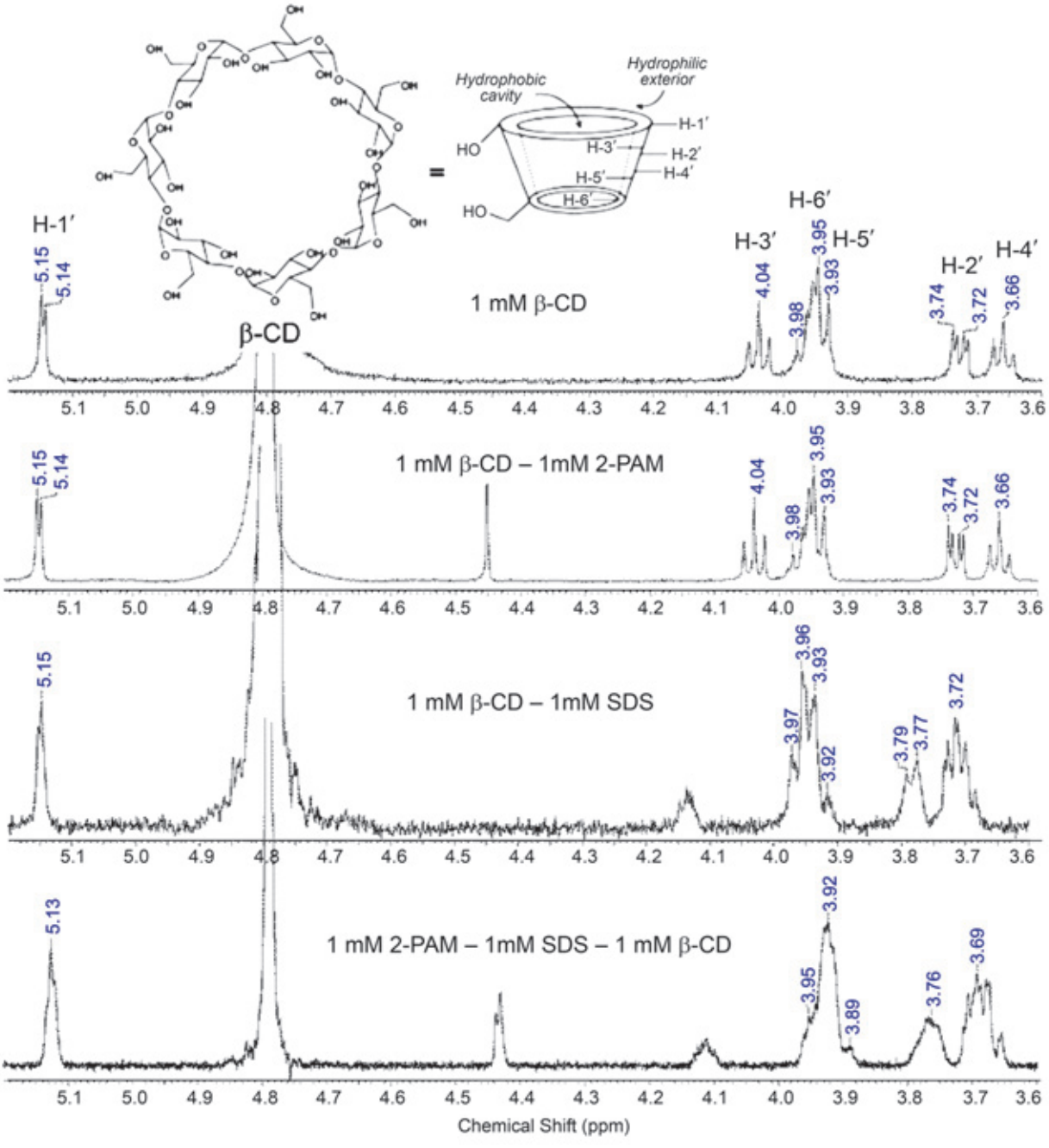

Figure 2. ^{1}H NMR spectra of 1 mM β-CD solution and its mixtures with 1 mM 2-PAM, 1 mM SDS and 1 mM 2-PAM–1 mM SDS, D_2O.

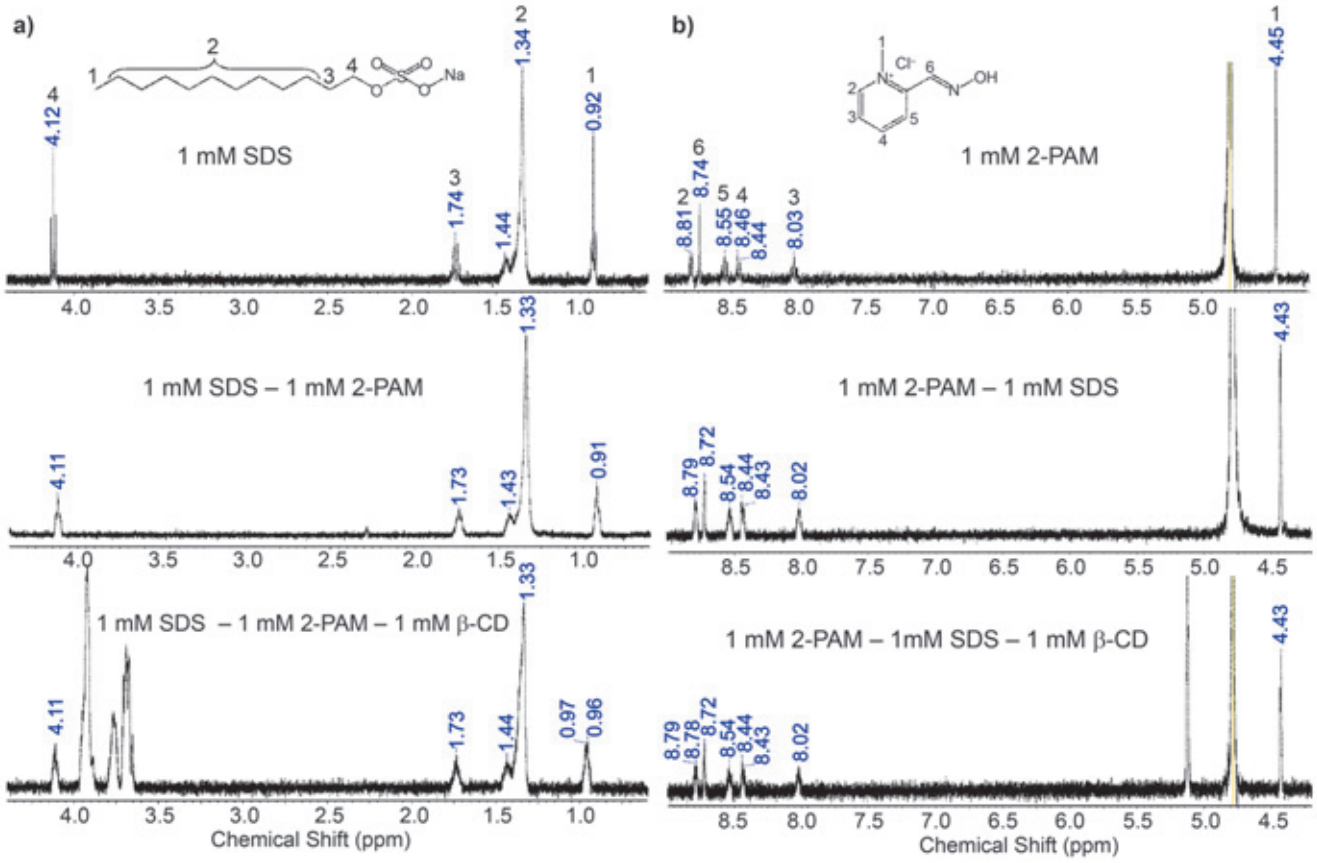

Figure 3. ^{1}H NMR spectra of 1 mM SDS (a) and 1mM 2-PAM (b) solutions and their mixtures, D_2O.

between SDS, 2-PAM and β-CD by means of ^{1}H NMR spectroscopy testifies the formation of a triple supramolecular system, the schematic structure of which is partially represented in Figure 4.

The micellar state of the supramolecular systems was also studied (Figure 5). ^{1}H NMR spectrum of binary SDS–2-PAM system shows that the SDS proton signals are upshifted, that is probably caused by promoting of SDS aggregation in the presence of 2-PAM due to the electrolyte effect. The interaction of SDS–2-PAM complex with β-CD causes a reverse downfield shift caused by the 'weakening' of the SDS aggregation in the presence of the macrocycle. By focusing on the zone corresponding to the aliphatic SDS protons, the signal of the intermediate methylene groups, which appears as a broad peak, is split into two or more signals. The downfield shifts and peaks broadening of these protons can be attributed to the Van der Waals effect and the polarity change of ambient environment which was caused by amphiphilic aggregation of surfactant in the presence of equimolar amounts of 2-PAM and β-CD. This result agrees with other studies, where the localization of part of the fraction of CDs in the SDS micelles was shown.[18,19]

We further looked how the pre-micellar and micellar form of the triple β-CD–SDS–2-PAM system affects the kinetics of POX hydrolysis. Spectrophotometric method was used to study the POX hydrolysis in equimolar solutions of various concentrations in PBS (p*H* 7.4). Since pK_a of 2-PAM is 7.68,[20] it is expected that buffer solution with

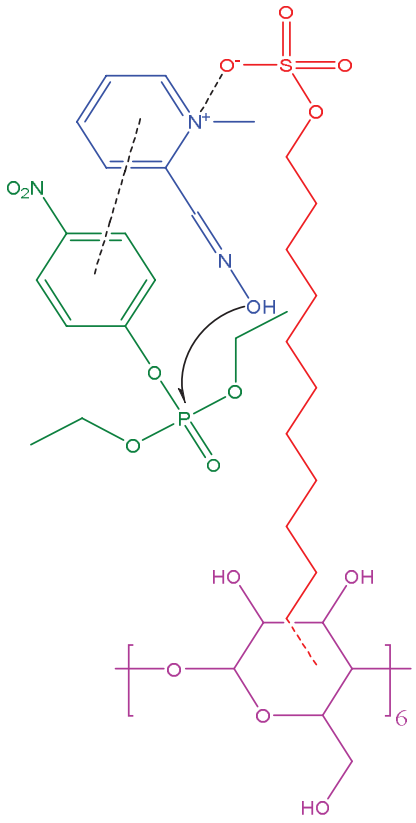

Figure 4. Supposed scheme of supramolecular interactions in the aqueous solution of SDS–2-PAM–β-CD–POX (dotted lines indicate interactions).

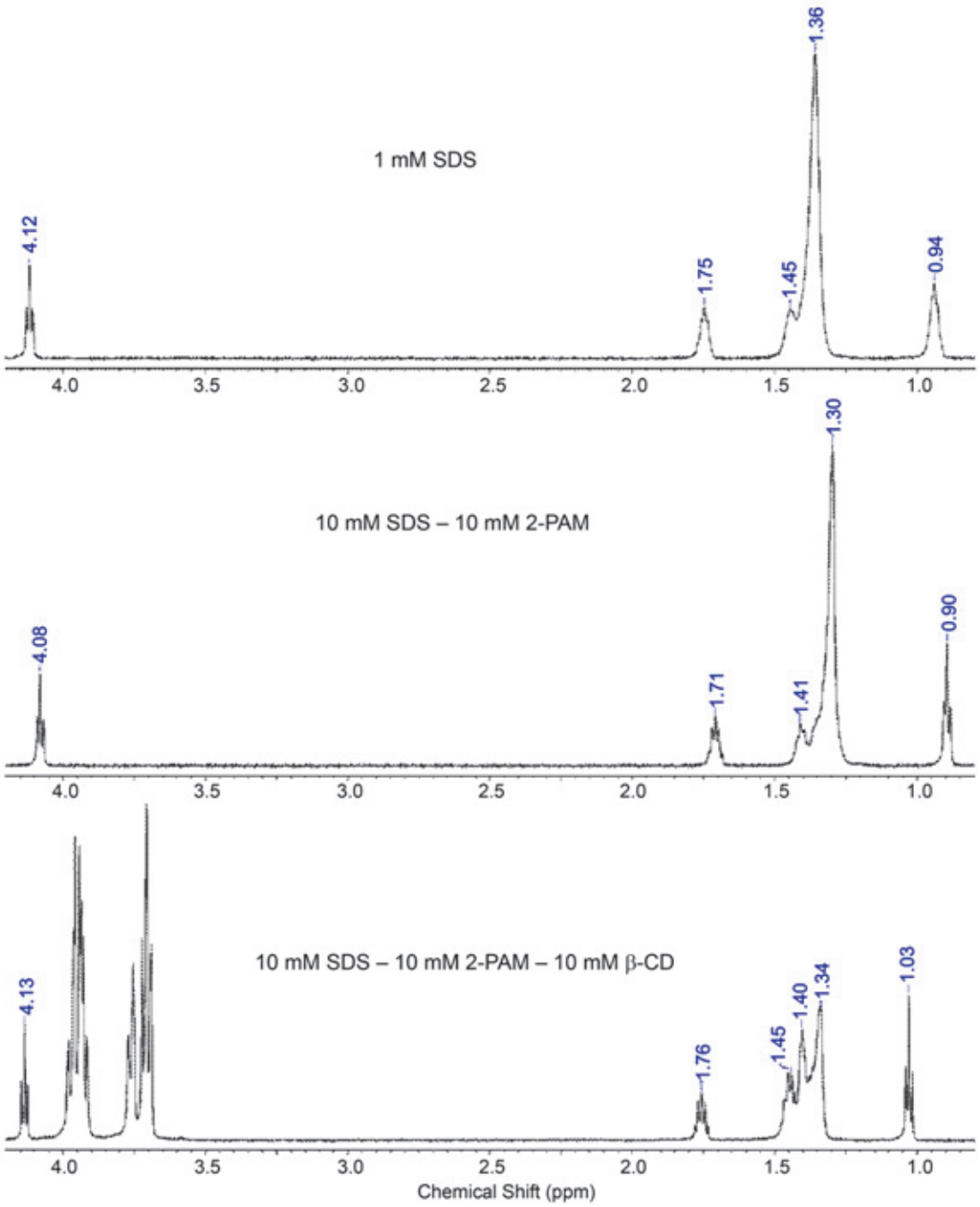

Figure 5. [1]H NMR spectra of 10 mM SDS solution and its mixtures with 10 mM 2-PAM and 10 mM 2-PAM–10 mM β-SDS, D_2O.

p*H* 7.4 will not provide a substantive content of the anionic (deprotonated) form of 2-PAM molecules that reveal reactivity towards esterolysis in contrast to the neutral species. A decrease in the fraction of this oxime form may weaken unfavorable repulsion from anionic micelles, thereby promoting their mutual affinity. However, there is a possibility that pK_a value for 2-PAM changes in micellar media of surfactants, but the study of surfactant influence on pK_a of oxime deserves a separate careful study and lies beyond the purpose of this work.

Figure 6 shows that the micellar structure of β-CD–SDS–2-PAM aggregates favours the concentration of reagents in the colloidal phase, *i.e.* transfer of POX from the solution to the hydrophobic part of aggregates. The hydrolysis constant in this triple system is slightly lower than in the single oxime solution with same amounts of 2-PAM. Probably, the main contribution to the acceleration of the reaction is made by oxime, and not by the macrocycle. It is known that the inclusion of the nitrophenoxyl part in the cyclodextrin cavity implies a sufficient affinity between the phosphorus atom and the secondary hydroxy groups, which promotes hydrolysis.[3] In our case, the macrocycle cavity is occupied by an alkyl chain of SDS, which prevents the binding of POX and causes a slight decrease in the rate constant. This is confirmed by [1]H NMR spectroscopy, where the largest chemical shift is observed for the aromatic proton near the oxime group in the triple system solution with POX (Figure 7). The revealed changes

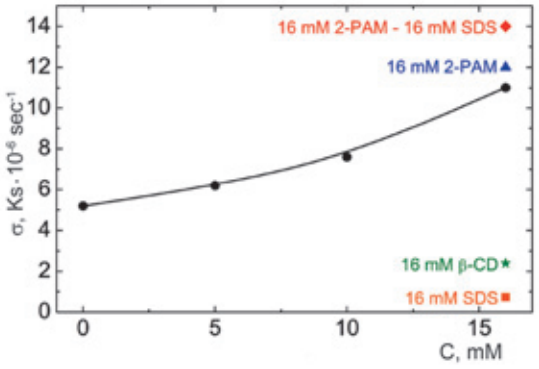

Figure 6. Concentration dependence of the observed rate constant for the POX hydrolysis in the aqueous equimolar system of SDS–2-PAM–β-CD (square, star, triangle and rhombic correspond to the observed rate constants of POX hydrolysis in individual 16 mM SDS, 16 mM β-CD, 16 mM 2-PAM solutions and mixed 16 mM 2-PAM–16 mM SDS solution), p*H* 7.4, 37 °C.

probably indicate the greater affinity of POX to oxime favoured by π-stacking interactions depicted in Figure 4. These π-stacking effects may additionally contribute to the dispersion forces realized between SDS micelles and POX.

Conclusions

In summary, a set of physicochemical methods were used to study supramolecular interactions in an aqueous system based on the surfactant SDS, oxime 2-PAM and macrocycle β-CD. We investigated the complexes of SDS with β-CD for binding 2-PAM. In this case, the surfactant molecule makes it possible to bind simultaneously two scavengers (namely oxime and cyclodextrin) able to trap and hydrolyze the paraoxon. This system accelerates the paraoxon hydrolysis, if it is in micellar form.

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References

1. Scherman O.A. *Nature Chemistry* **2009**, *1*, 524–525.
2. Zakharova L., Mirgorodskaya A., Zhiltsova E., Kudryavtseva L., Konovalov A. Reactions in Supramolecular Systems. In: *Molecular Encapsulation: Organic Reactions in Constrained Systems*. United Kingdom: John Wiley & Sons, **2010**. p 397–420.

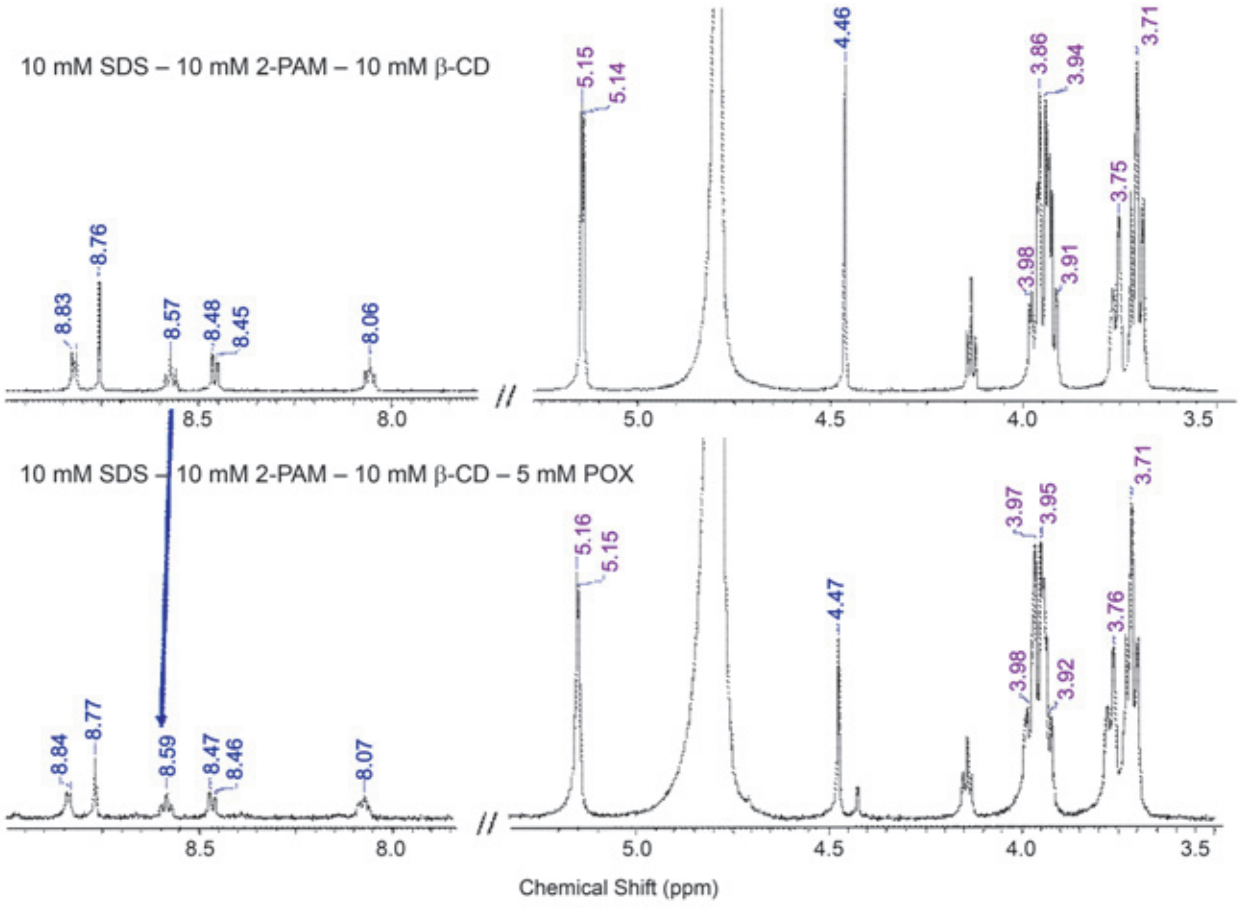

Figure 7. ^{1}H NMR spectra of 10 mM SDS–10 mM 2-PAM–10 mM β-CD in the absence and presence of 5 mM POX (D_2O, p*H* 6.8). The arrow indicates the largest change in the chemical shift of the proton 5 of 2-PAM.

3. Letort S., Balieu S., Erb W., Gouhier G., Estour F. *Beilstein J. Org. Chem.* **2016**, *12*, 204–228.
4. Westheimer F.H. *Science* **1987**, *235*, 1173–1178.
5. Kanagaraj K., Affrose A., Sivakolunthu S., Pitchumani K. *Biosens. Bioelectron.* **2012**, *35*, 452–455.
6. Zhao H., Ji X., Wang B., Wang N., Li X., Ni R., Ren J. *Biosens. Bioelectron.* **2015**, *65*, 23–30.
7. Ramaseshan R., Sundarrajan S., Liu Y., Barhate R.S., Lala N.L., Ramakrishna S. *Nanotechnology* **2006**, *17*, 2947–2953.
8. Mirgorodskaya A.B., Yackevich E.I., Kudryashova Y.R., Kashapov R.R., Solovieva S.E., Gubaidullin A.T., Antipin I.S., Zakharova L.Y., Konovalov A.I. *Colloids Surf., B* **2014**, *117*, 497–504.
9. Zhiltsova E.P., Syakaev V.V., Lukashenko S.S., Timosheva A.P., Kashapov R.R., Latypov Sh.K., Zakharova L.Ya., Konovalov A.I. *Fluid Phase Equilib.* **2013**, *360*, 16–22.
10. Gaynanova G.A., Vagapova G.I., Valeeva F.G., Vasilieva E.A., Galkina I.V., Zakharova L.Ya., Sinyashin O.G. *Colloids Surf., A* **2016**, *489*, 95–102.
11. Gabdrakhamanov D.R., Samarkina D.A., Semenov V.E., Saifina L.F., Valeeva F.G., Reznik V.S., Zakharova L.Ya. *Phosphorus, Sulfur Silicon Relat. Elem.* **2016**, *191*, 1673–1675.
12. Sharma R., Gupta B., Yadav T., Sinha S., Sahu A.K., Karpichev Y., Gathergood N., Marek J., Kuca K., Ghosh K.K. *ACS Sustainable Chem. Eng.* **2016**, *4*, 6962–6973.
13. Ghosh K.K., Tiwari S., Marek J., Kuca K. *Main Group Chem.* **2010**, *9*, 337–353.
14. Kandpal N., Dewangan H.K., Nagwanshi R., Ghosh K.K., Satnami M.L. *J. Mol. Liq.* **2017**, *243*, 178–186.
15. Valente A.J.M., Söderman O. *Adv. Colloid Interface Sci.* **2014**, *205*, 156–176.
16. Berezin I.V., Martinek K., Yatsimirski A.K. *Russ. Chem. Rev.* **1973**, *42*, 787–802.
17. Samarkina D.A., Gabdrakhmanov D.R., Semenov V.E., Valeeva F.G., Nikolaev A.E., Saifina L.F., Zakharova L.Ya. *Russ. J. Gen. Chem.* **2017**, *87*, 1977–1984.
18. Fajalia A.I., Tsianou M. *Colloids Surf., A* **2015**, *480*, 91–104.
19. Tsianou M., Fajalia A.I. *Langmuir* **2014**, *30*, 13754–13764.
20. Kalisiak J., Ralph E.C., Zhan J., Cashman J.R. *J. Med. Chem.* **2011**, *54*, 3319–3330.

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