Investigation into the Sphere to Rod Micellar Transition of the 12-3-12 Br Gemini Surfactant in the Presence of Sodium, Para-fluorobenzoate

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Abstract

Investigation into the use of sodium, para-fluorobenzoate (p-FB) as a 12-3-12 Br Gemini surfactant counter ion was studied. The critical micelle concentration of the 12-3-12 Br surfactant was determined to be 1.0221mM using fluorescence and conductivity measurements. Varying solutions of Na^+, p-fluorobenzoate from 0 to 10 mM in 2mM increments were prepared in a constant 10 mM 12-3-12 Br surfactant solution. Solutions of Na^+, p-fluorobenzoate from 0 to 20 mM in 4 mM intervals were prepared in a constant 20 mM 12-3-12 Br surfactant solution. Viscosity changes were noted in each series of solution and rod-like micelles were formed from 8mM to 12mM in the 20mM series and 4mM to 8mM in the 10mM series. Chromatograms were generated from running these solutions on HPLC-UV. Peak areas in the chromatograms were then compared to a series of standards in order to determine the interfacial concentrations of varying species at the interface. The data obtained suggests that the use of para-fluorobenzoate produces a stabilizing effect upon the formation of rod-like micelles of the 12-3-12 Br surfactant.

1. Introduction

Surfactants have been known to have unique interfacial and bulk properties that have uses in a wide variety of applications.[a] Changes in their structure in order to enhance the effectiveness of the molecules has drawn the interest of chemists in the recent past and has lead to the development of Gemini surfactants.[b,c,d,e] The two surfactants, conventional and Gemini, differ in that conventional surfactants contain one single hydrophobic tail that is connected to an ionic or polar head group. Gemini surfactants have a hydrophobic tail connected to a polar or ionic head group connected to a spacer group that is connected to a second polar head group and hydrophobic tail. Gemini surfactants are known to be more surface-active than conventional surfactants and are thus, a good model to study.[a] Increasing the surface activity means that a lower concentration of surfactant is required to perform a necessary function. The lower CMC, or critical micelle concentration, of geminis produce less skin irritation, typically depending upon the concentration of surfactant monomer in solution.[i] In Gemini surfactants, structure is represented by m-s-m, where m is the number of alkyl carbon atoms on the surfactant tails and s is the number of carbons in the spacer group separating the quaternary nitrogen atoms.

Critical micelle concentration (CMC) is the concentration above which monomeric surfactant forms micellar aggregates. Hydrophobic interaction opposed by electrostatic repulsion among the ionic head groups drives this process of micellization[b].

Surfactant properties such as solubilization are very important phenomena that are required in tertiary oil recovery and detergency, as both are involved in process of homogenizing solutions. Research has shown that cationic geminis are better solubilizers than conventional surfactants due to the tubular shape of the aggregates.[h]

The antimicrobial properties of surfactants depend on the length and type of spacer and the hydrophobic component of the molecule. Quaternary ammonium salts, such as the one utilized throughout this project, are typically known as disinfectants. A nonionic gemini surfactant is found to be non-irritating and non-hemolytic, and is suitable for use in personal care and pharmaceutical formulations, proving the effectiveness of geminis in medicinal chemistry.[i] In contrast to corresponding single-chain molecules, two alkyl chains in one molecule linked by a spacer chain enhance the adsorption and aggregation properties by strengthening the intra or intermolecular hydrophobic interactions.[i] The various applications of surfactants make them a good model to study in that the chemical phenomena of these molecules is not completely understood at this moment. Additionally, the need to influence these molecules to perform in solution can have drastic impacts on the industrial production and

engineering of these molecules. This research represents an attempt at understanding these vastly unique and not-fully-understand class of compounds.

It is known that the introduction of ions into micellar solutions produces rod-like micelles. This process is noted by the figure at the left. However, this research focuses on the ability of aromatic counterions, specifically para-fluorobenzoate, to stabilize the formation of rod-like micelles in the 12-3-12 Br surfactant. This phenomenon can be analyzed by HPLC-UV (high performance liquid chromatography). Specifically, the method utilized was the trapping method similar to the trapping methods utilized by Dr. Romsted at Rutgers University. This procedure is summed up by the figure below. The black circles or, ions present at the interface of the micelle, can be determined utilizing peak areas under the chromatograms generated from the HPLC. Utilizing this data, it can be deduced which ions present in the solution are contributing to the stabilization of the rod-like micelle and not simply present in bulk solution.

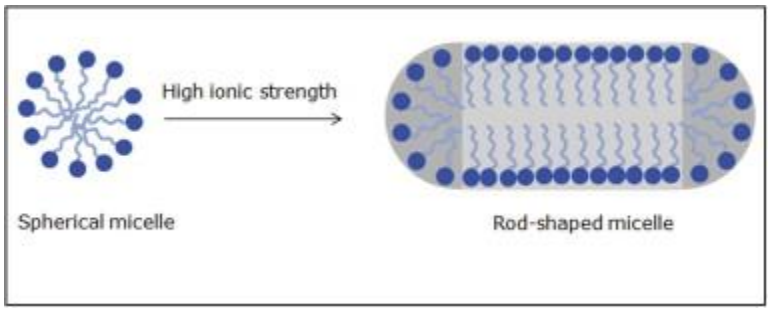

Figure 1: The addition of salts stabilize the formation of rod-shaped micelles.[K]

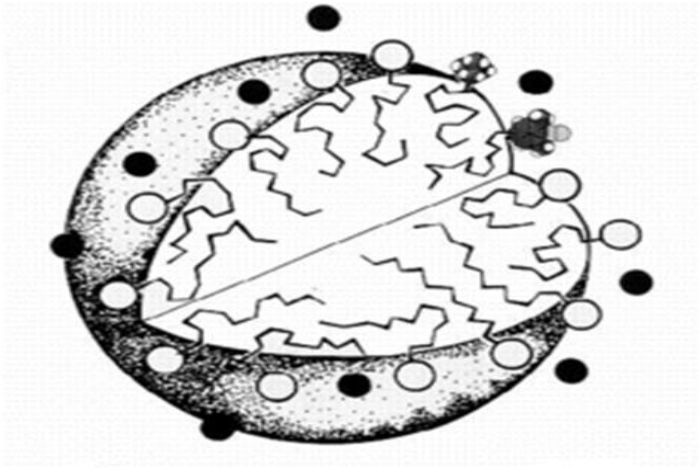

Figure 2: Diagram of the chemical trapping experiment. The white circles with tails represent typical surfactants, the white and black circle represents the diazonium ion, or trapping agent, and the black circles represent the various ions present at the interface of the spherical micelle.[I]

2. Methods & Materials

2.1 Synthesis

Many of the methods described below were followed according to procedures undertaken in Lanzhen's thesis.

2.1.1 Synthesis of 4-n-Hexadecyl-2,6-dimethylphenol, 16-ArOH (I)

25mL's of H_2O was added dropwise to a solution of .5742g 16-ArN_2BF_4 in 25mL's of THF under N_2 atmosphere. The mixture was stirred overnight at room temperature and two layers – organic and aqueous- were formed. After extracting the bottom aqueous layer and removing the solvent, the solid was dissolved in MeOH and its purity was checked by GC-MS. The reaction afforded mostly 16-ArOH but was contaminated with significant 16-ArF. Column chromatography was performed (eluent: Hexane: EtOAc = 10:1, R_f=0.49 for 16-ArOH) to obtain .10 g pure 16-ArOH checked by GC-MS.

2.1.2 Synthesis of 4-n-Hexadecyl-2,6-dimethylphenol, (16-ArOH) (II) and 4-n-Hexadecyl-2,6-dimethylbromobenzene (16-ArBr)

Both products were synthesized simultaneously by carrying out the dediazoniation reaction of IIb in aqueous (CTA)Br micelles and 0.1 M HBr with 4.0 M added NaBr to enhance the yield of the bromo

product. A mixture of 205.8 g of NaBr (2 mol; 99+% ACS grade, Fischer), 18.22 g (0.05 mol) of (CTA)Br (freshly recrystallized), 50 mL of 1.0 M HBr, and 450 mL of water, which gave final molarities of 4.0, 0.1, and 0.1 M, respectively, was placed in a 1-L three-neck round-bottom flask and heated with stirring for about 1 hour at 60°C in a water bath to dissolve the reactants; 2.5 g of IIb was added, and cooled to room temperature, and 10.54 g (0.075 mol) of $NaClO_4 \cdot H_2O$ in 100 mL of H_2O was added; the heavy, white precipitate of $(CTA)ClO_4$ and other products were collected on a Buchner funnel, washed with H_2O several times, and air (2 hours) and vacuum-dried (24 hours). The precipitate was ground to a fine powder and extracted with about 250 mL of Et_2O with vigorous stirring (15 minutes), and the extract was filtered three times. Rotoevaporation of the combined extracts gave a white solid (1.9 g, 75%) which showed two spots by TLC (SiO_2, 90% hexane/10%EtOAc v/v; R_f = 0.23 and 0.74). The mixture was chromatographed on a 40 mm x 135 mm column containing silica gel (80 g; 70-230 mesh, Aldrich) and eluted first with pure hexane to remove 16-ArBr (R_f = 0.74) as a white low melting point solid (0.93 g, 40.4%; mp 39°C) and then with 20% EtOAc/hexane (v/v) to remove 16-ArOH as a pale yellow solid (R_f = 0.23). Two consecutive Norit treatments of 16-ArOH in MeOH gave 0.25 g (12.8%) of white crystals, mp 76°C.

2.1.3 Synthesis of 5-hexadecyl-7-methylindazole

2.6 g (7.13 mmol) hexadecyl trimethyl ammonium bromide (CTAB) was dissolved in 500 mL 20 mM aqueous phosphate buffer (pH 7.0) to prepare a cationic micellar solution. 110 mg (0.25 mmol) of 16-$ArN_2^+BF_4^-$ dissolved in 10 mL HPLC grade acetonitrile was added to the micellar solution and the solution was kept stirred overnight (12 hours). The solution turned light yellow, and 1.5 g (10.7 mmol) of sodium perchlorate monohydrate was added to this yellow solution. Immediately, a heavy white precipitate appeared. The precipitate was filtered and washed with a copious amount of water. The washed precipitate was air-dried using a water aspirator for 4 hours and finally the air-dried precipitate was vacuum-dried for 2 hours. The dried precipitate was then extracted with ether (3x200 mL). The combined ether extract was dried with anhydrous sodium sulfate and filtered. The ether was removed from the filtrate using a rotary evaporator and 16-Ind was isolated from the residue by silica gel column chromatography, changing the eluent from pet-ether to pet-ether/ethyl acetate (88:12, v/v). The fractions with R_f = 0.6 (using 60:40 pet-ether/ethyl acetate, the TLC developing solvent) were combined and the solvent was evaporated. The white residue left after evaporation of the solvent afforded 50 mg of pure 16-Ind (57% yield) upon crystallization from acetone.

2.1.4 Synthesis of 4-n-Hexadecyl-2,6-dimethylfluorobenzene

Residual diazonium was placed in a sealed glass vial. The vial was placed in a solution of H_2O that was heated to 40°C-60°C for one hour. After cooling the vial was opened and toxic vapor diffused from the chamber. The resulting gray powder was run in GC-MS and the decomposition product was successfully isolated.

2.1.5 Synthesis of 4-n-Hexadecyl-2,6-dimethylbenzenediazonium Tetrafluoroborate, 16-ArN_2BF_4

About 15 mL's of THF was injected into a three-necked 100-mL round-bottom flask fitted with a 25-mL dropping funnel, septa, and a magnetic stir bar, the system was cooled (10 min) in a dry ice/isopropyl alcohol bath, 2.0 mLs of $BF_3 \cdot Et_2O$ (Aldrich, fresh) was added by syringe, and the mixture was stirred for 5 minutes. 3g of 16-$ArNH_2$ dissolved in 15 mL of THF was added via syringe, resulting in a clear solution. 2.0 mL of *tert*-butyl nitrite (Aldrich, fresh) in 15 mL of THF was added to the dropping funnel and added to reaction vessel over a 2-min period. After 20 min of stirring the temperature was increased to 0°C and the solution was stirred for 6h. The reaction mixture was transferred to a 500-mL beaker and 100 mL of cold pentane added; the off-white solid was collected on a Buchner funnel, recrystallized three times by dissolving it in CH_3CN (Fischer, HPLC grade) and forced from solution with cold anhydrous Et_2O. Upon

addition of the Et_2O, the solution was placed in a dry ice/isopropyl alcohol bath. The resulting off-white solid was collected on a Buchner funnel and yielded 1.5573g of diazonium product.

2.1.6 Synthesis of 12-3-12 Br Gemini surfactant

19.27mL Bromodecane was added to 30mL acetone, 3.66 mL of N,N,N',N'-tetramethylpropanediamine (TMPD) was added, followed by 7.5mL acetone and was refluxed for 24 hours. A white powder precipitated from the mixture, was dissolved in acetone, vacuum filtered and let dry overnight. The resulting white powder was recystallized by adding 250mL's of acetone, heated to 120°C and cooled in an ice bath to yield 15.768g of 12-3-12 Br surfactant. The resulting surfactant was stored in a dessicator for later use.

2.1.7 Synthesis of 4-n-Hexadecyl-2,6-dimethylbenzeneaniline

A mixture of 1-hexadecanol (70.31 g, 0.29 mol; Aldrich, freshly vacuum distilled), and $ZnCl_2$ (57.24 g, 0.42 mol; Aldrich, fresh, anhydrous) was placed in a 1-L, three-neck round-bottom flask fitted with a heating mantle, stirrer, Dean-Stark trap, and thermometer and heated under dry N_2 at 260°C for 21 hours. On refluxing, the reaction mixture turned violet. It was then cooled to room temperature, transferred to a 2-L beaker in an ice bath, and acidified with excess 2.35 N H_2SO_4 to destroy the $ZnCl_2$·aniline complex, followed by neutralization with concentrated NH_4OH. A yellow-brown oil separated from the mixture, and the aqueous phase was extracted with Et_2O three times; the combined oil and Et_2O extracts were dried over NaOH pellets. Excess Et_2O was removed on a rotary evaporator, and the excess 2,6-dimethylaniline was removed by vacuum distillation. Five successive treatments of the brown semisolid residue with Norit in hot MeOH followed by recrystallization from MeOH gave 18 g of yellow crystals.

2.1.8 Synthesis of sodium 4-fluorobenzoate salt

6.0465 g of 4-fluorobenzoic acid was dissolved in 200 mL's H_2O.The resulting solution was titrated using a standardized solution of 0.0933 M NaOH to a pH of 7.0. The solution was then evaporated on a heating mantle (120-160°C) until a white powder precipitated from the mixture. The powder was scraped using a spatula to obtain 7.1080 g of sodium, 4-fluorobenzoate salt.

2.2 Other Methods

Other methods were useful in the process of determining the species present at the interface of the micelle. These methods included ^1H NMR, GC-MS, HPLC, UV- diode array, fluorimetry, and conductivity.

3. Results and Discussion

3.1 Critical Micelle Concentration (CMC) determination

3.1.1 CMC determination by fluorescence

A stock solution of dichlorofluoroscein was prepared by dissolving 0.0473g dichlorofluoroscein in 250mL of deionized H_2O. A 1:5 dilution of this solution was used for all resulting fluorescence measurements. A series of 12-3-12 Br surfactant was added to a total volume of 25mL in volumetric flasks with a consistent 5.00mL of dichlorofluoroscein added to each flask. A series of 13 samples was made ranging from 0-1.6mM 12-3-12 Br surfactant. The following graph was compiled using the fluorimeter measurements generated from this process.

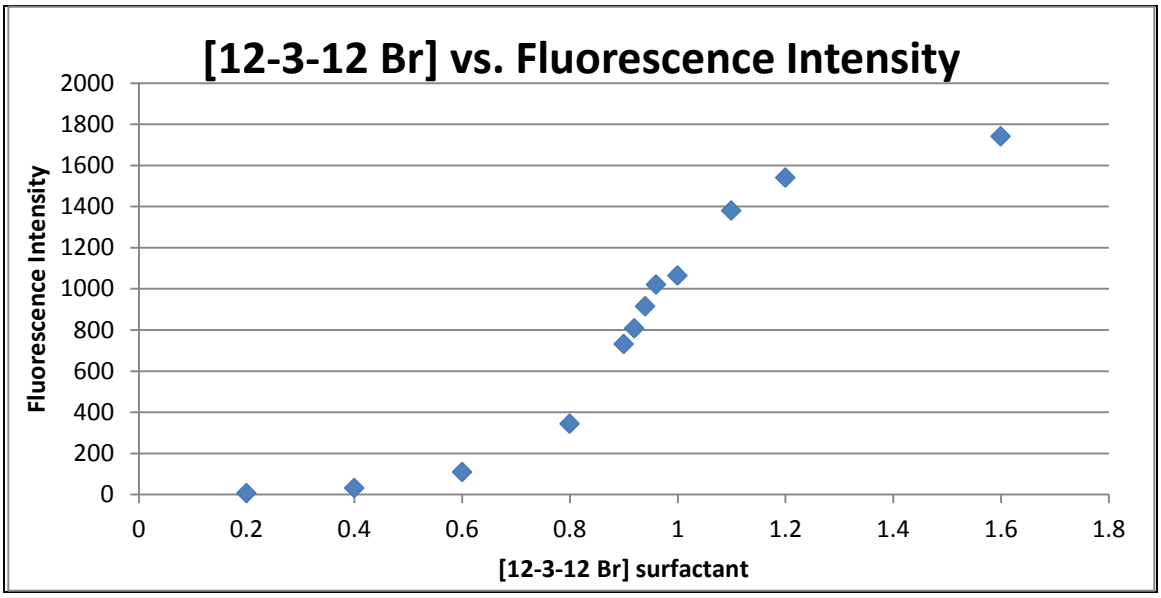

Figure 3: Fluorescence intensity was measured as the [12-3-12 Br] was increased.

3.1.2 CMC determination by conductivity

Conductivity was measured by preparing a series of various concentrations of 12-3-12 Br surfactant beginning at 0 mM to 2.75 mM. The following figure was prepared by using these measurements.

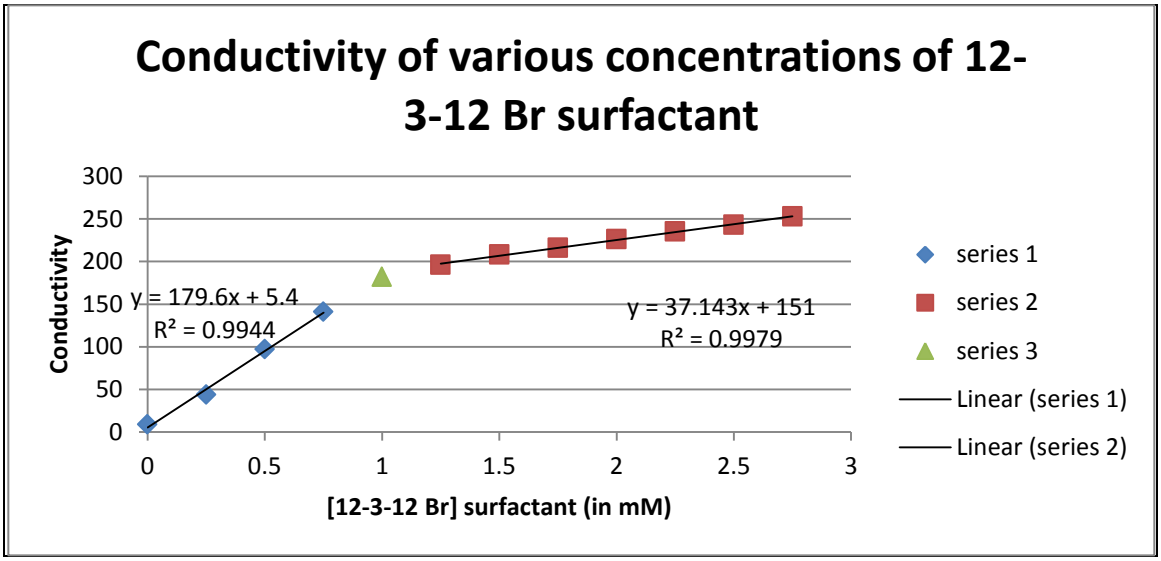

Figure 4: A series of concentrations of 12-3-12 Br surfactant (0-2.75mM) in H2O was measured for conductivity in order to determine the CMC.

3.2 Calibration Curves

Calibration Curves were generated for the phenol, fluoro and bromo product in order to determine retention times and interfacial concentrations. Figures 5,6, and 7 are the curves generated from these efforts.

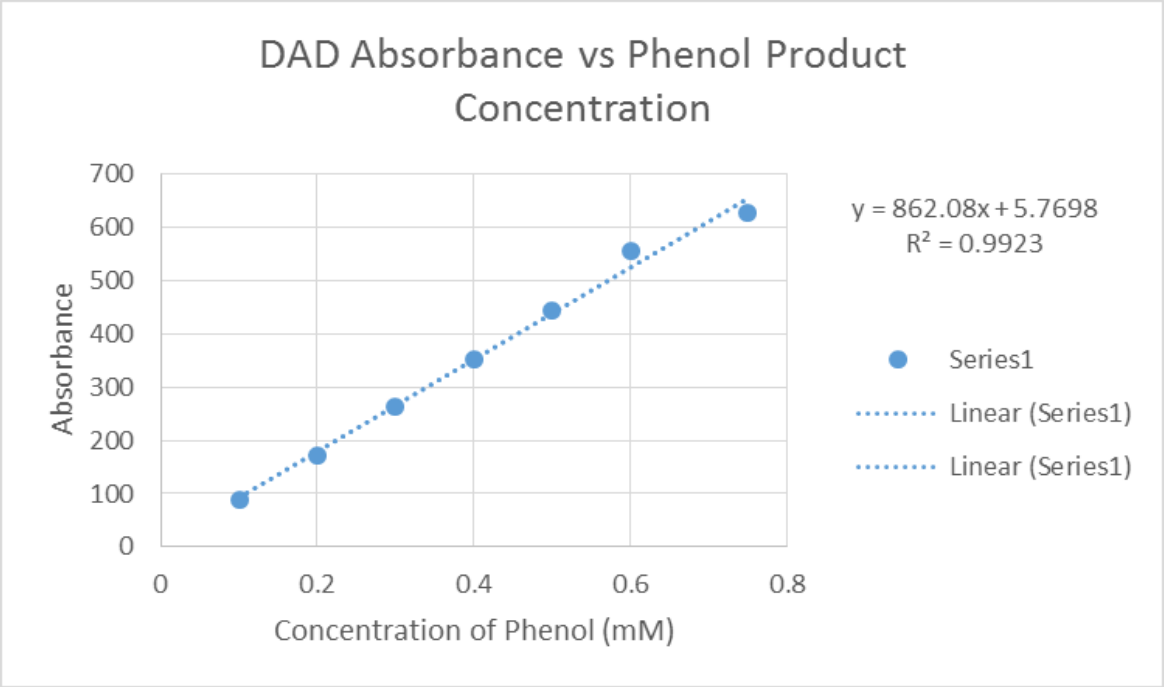

Figure 5: A calibration curve was attained utilizing the phenol standards run under the same methods on the HPLC as the trapping experiment (λ= 280nm).

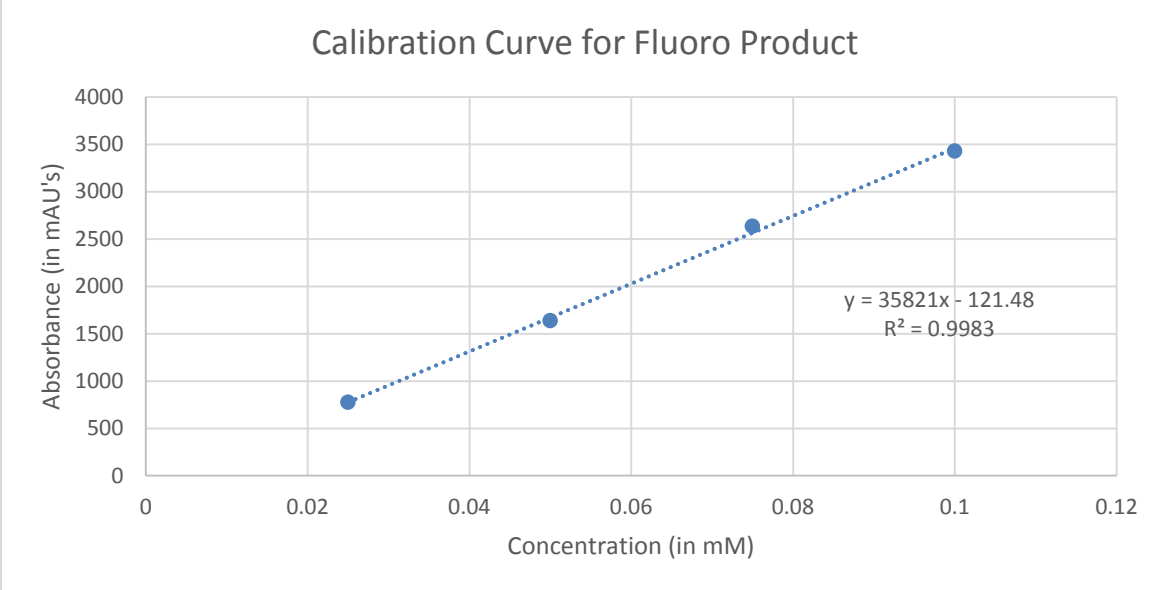

Figure 6: A calibration curve was attained utilizing the phenol standards run under the same methods on the HPLC as the trapping experiment. (λ= 280nm).

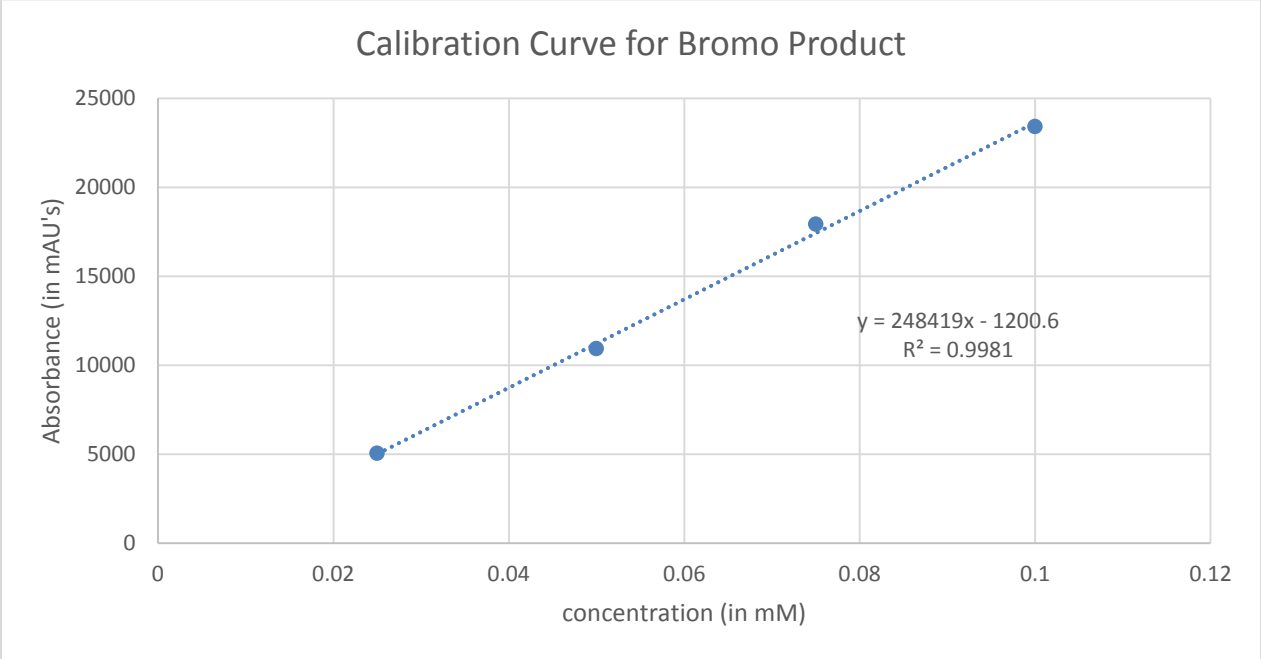

Figure 7: Figure 6: A calibration curve was attained utilizing the phenol standards run under the same methods on the HPLC as the trapping experiment (λ= 280nm).

3.3 Trapping Experiments

3.3.1 12-3-12 Br Trapping at 10 mM p-Fluorobenzoate

Determination of interfacial Concentrations For 10mM trapping:

The following interfacial concentrations were determined by plugging the peak areas from each addition of p-FB salt into the equations generated from the calibration curves. Each of the following concentrations was done for the fluoro, and bromo products. Further calculations and efforts are needed for the determination of the interfacial concentrations of other species in solution. However, general observations can be made by noting large changes in peak area for certain samples. For 2mM p-FB salt and 10mM 12-3-12 Br surfactant the fluoro and bromo concentrations were .00438 and .00619 (in mM), respectively. For 4mM p-FB salt, under the same conditions, the fluoro and bromo concentrations were.00489 and .0063 (in mM), respectively. For 6mM p-FB salt, under the same conditions, fluoro and bromo concentrations were .00511 and .0062 (in mM), respectively. For 8 mM p-FB salt, under the same conditions, the fluoro and bromo concentrations were, .00551 and .0062 (in mM), respectively. For 10 mM p-FB salt, under the same conditions, the fluoro, and bromo concentrations were .00566 and .0063 (in mM), respectively. Although, not very noticeable on the graph shown, it is believed that the interfacial concentration of the ester product (shown as 7 on the chromatogram) can be seen to be increasing in peak area once the peaks are standardized. This is indicative of the aromatic counterion stabilizing the micelle as the concentration of the ion is increased in solution. It is possible that the three methyl linking group is just large enough for the aromatic counterion to sit in the pocket between the two charged head groups. This special pocket could be the reason for the noted increase in stabilization of the rodular micelle as noted from the observed viscosities of the solutions. The concentrations of phenol product in the 10mM trapping experiments can be seen to be decreasing as the concentration of the p-fluorobenzoate is increased in a linear fashion. This supports the idea that hydration of the micelle is decreasing as the concentration of the salt is added. The aromatic counter-ion placed in the system is then believed to be the supporting species of the rod-like micelle in solution as the concentration of salt is increased. When compared to the observational results obtained upon successive addition of the p-fluorobenzoate salt to a constant concentration of 10 mM of 12-3-12 Br surfactant, it is observed that rod-like micelles are formed as the concentration of the salt is increased. The data then suggests that the added salt is

interacting with the system to decrease the hydration of the micelle and stabilize the formation of rod-like micelles.

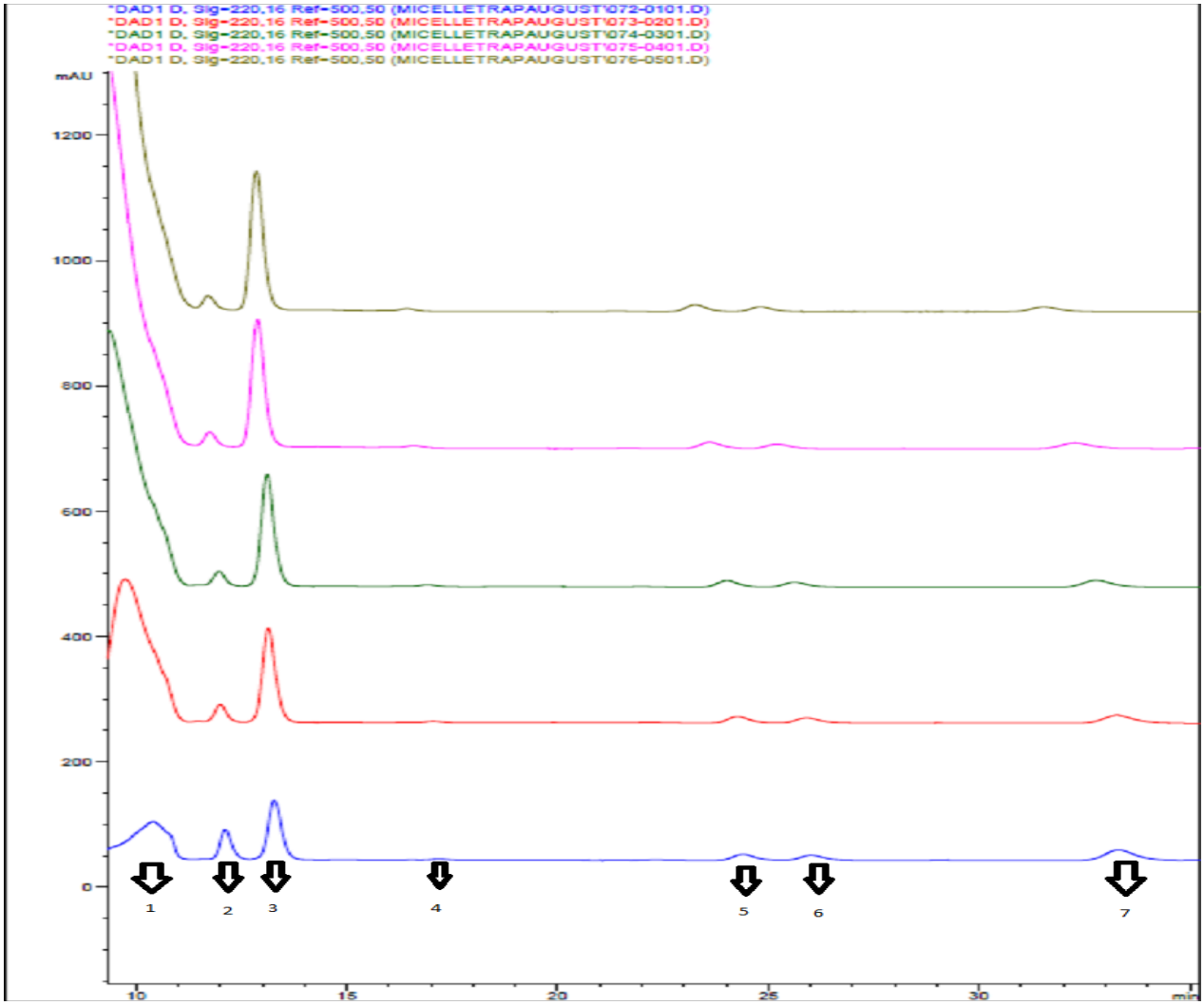

Figure 8: The trapping experiment was done at a constant 10 mM concentration of 12-3-12 Br surfactant and at 2mM p-FB (blue), 4 mM p-FB (red), 6mM p-FB (green), 8mM p-FB (pink), and 10mM p-FB (dark green). Peak retention times were assigned based on the previous standards and interfacial concentration were determined from calibration curves previously generated. Identification of peaks: 1= excess effluent of aromatic counterion, 2=phenolic product, 3=indazole product, 4= fluoro product, 5= bromo product, 6= unidentified product, & 7= ester product.

3.3.2 12-3-12 Br Trapping at 20 mM p-Fluorobenzoate

Determination of interfacial Concentrations For 20mM trapping:

The following interfacial concentrations were determined by plugging the peak areas from each addition of p-FB salt into the equations generated from the calibration curves. Each of the following concentrations was done for phenol products only. Additional data and calculations are needed for exact determination of other species in solution. For the 4mM trapping experiments, the phenol product concentration was 1.83mM. For the 8mM trapping experiments, the phenol product concentration was .803mM. For the 12mM trapping experiments, the phenol product concentration was .977mM. For the 16mM trapping experiments, the phenol product concentration was .969mM. For the 20mM trapping experiments, the phenol concentration was indeterminable

due to tailing in the chromatogram. Both the fluoro and bromo product interfacial concentrations were indeterminable due to differences in retention times from the fluoro and bromo standard retention times and the 20 mM trapping experiments. However, it is clear that the hydration of the micelle is decreasing significantly as the concentration of the added salt is increased. These results are consistent with the results generated from the 10 mM trapping experiments. Although certain species were indeterminable the results still suggest that p-Fluorobenzoate is an effective facilitator of rod-like micelles in the 12-3-12 Br gemini surfactant solution. Once again, the p-FB ion has been seen to decrease the hydration of the micelle as more of it is added to bulk solution. Although the reasons for the extra affinity for the micelle can be speculated upon, it is clear that a significant amount of the salt is present at the interface and inducing viscoelastic changes in solution. These changes in viscoelastic properties, coupled with the data generated from the two trapping experiments indicate that p-Fluorobenzoate could be used to induce sphere to rod-like transitions in micelles for future applications.

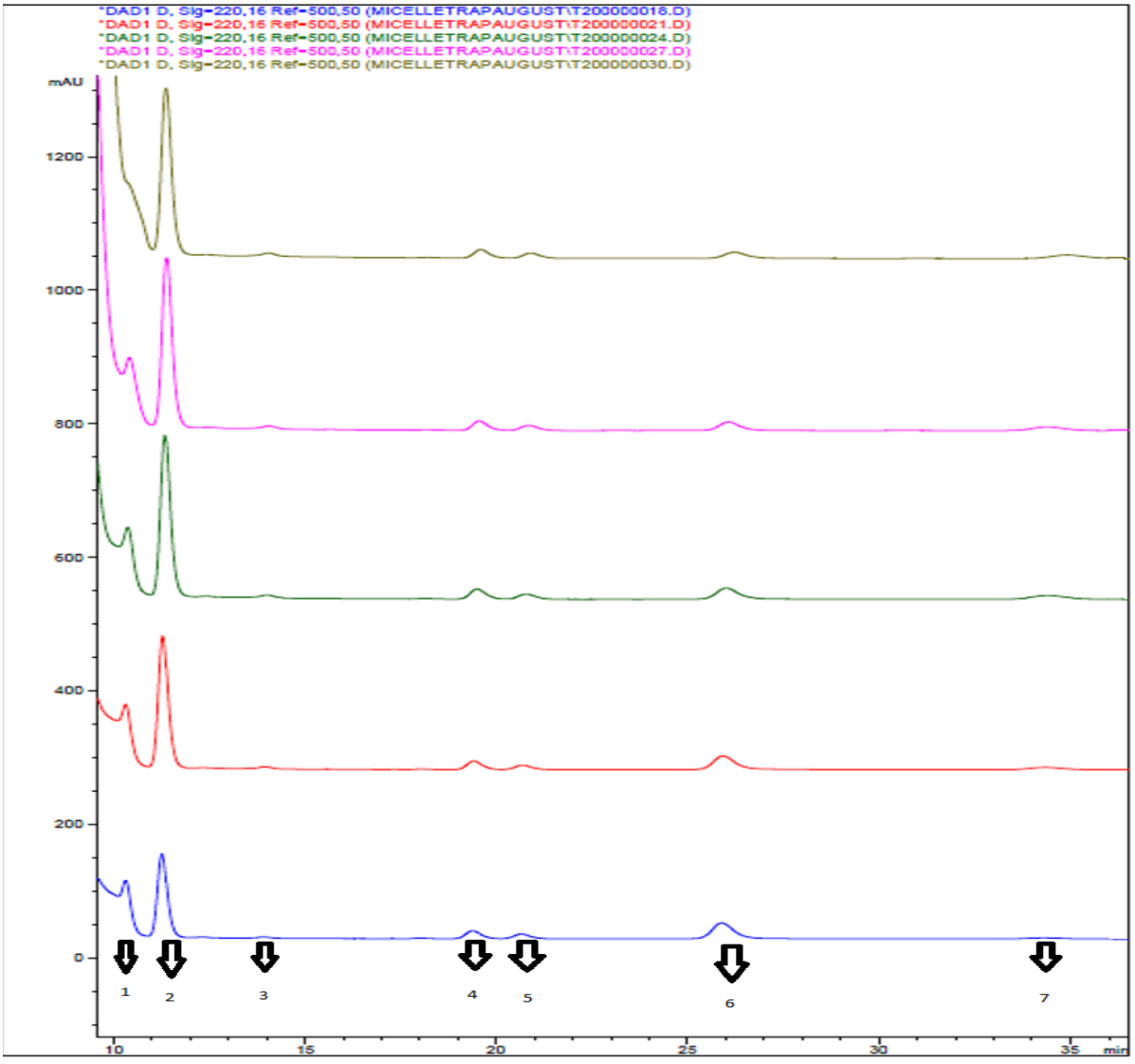

Figure 9: The trapping experiment done at a constant 20mM concentration of 12-3-12 Br surfactant and at 4mM p-FB (blue), 8mM p-FB (red), 12mM p-FB (green), 16mM p-FB (pink), and 20mM p-FB (black). Peak retention times were assigned based on the standards previously described and interfacial concentrations were determined from calibration curves previously generated. Identification of peaks from standards: 1= phenol product, 2= indazole product, 3= unknown, 4= fluoro product, 5= bromo product, 6= ester product & 7=unknown.

Conclusion

The data generated supports that the p-fluorobenzoate counterion is stabilizing the formation of rod-like micelles. It is speculated that the three methyl spacer group is just the right size for the negatively-charged aromatic counterion to sit in and stabilize the positively charged head group in the micelle. However, in order to have more utilizable data, the samples would be best to run on an LC-MS. This would allow for proper identification of peaks and would significantly decrease the risk of improper peak assignments. Additional runs of the samples are necessary in order to standardize the data and give more consistent peak retention times as well as utilizable quantitative data. This data would allow us to further characterize some of the species are present at significant quantities at the interface. Overall, the data suggests that there is an interesting chemical phenomenon that is occurring upon introduction of the aromatic counterion into surfactant solution that may have future applications for engineering or industrial endeavors.

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References

a. Paul, B.K. and Moulik, S. P., *ibid*, 2001, **80**, 990-1001
b. Nierderl, J. B. and Lanzilotti, A. E., *J. Am. Chem. Soc.*, 1944, **66**, 844-852.
c. Bunton, C. A., Robinson, L., Schaak, J. and Stern, M. F., *J. Org. Chem.*, 1971, **36**, 2346-2350.
d. Devinsky, F., Masarova, L. and Lacko, L, *Colloid Interface Sci.*, 1985, **105**, 235-239.
e. Zhu, Y. P., Masuyama, A. and Okahara, M., *J. Am. Oil Chem. Soc.*, 1990, **67**, 459-463.
h. Engberts, J. B. F. N., Dam, T., Karthauser, J., Karaborni, S. and van Os, N. M., *Colloids Surf. A*, 1996, **118**, 41-47.
i. Macian, M., Seguer, J., Infante, M. R., Selve, C. and Vinardell, M. P., *Toxicology*, 1996, **106**, 1-9.
k. Chaudhuri, A. et. Al. Organization and dynamics in micellar structural transition monitored by pyrene fluorescence. Biochemical and Biophysical Research Communications. Volume 390, issue 3, 18 December 2009, pages 728-732.
l. Romsted, S Lawrence. Composition of Aggregates by Chemical Trapping. http://chem.rutgers.edu/romsted_laurence_s. (Accessed Summer 2013).