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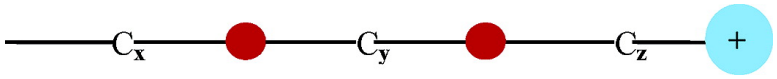
J. Am. Chem. Soc., **2004**, 126 (48), 15883-15889• DOI: 10.1021/ja040105s • Publication Date (Web): 11 November 2004



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Contiguous versus Segmented Hydrophobicity in Micellar Systems

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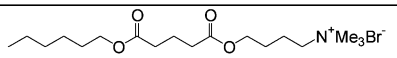
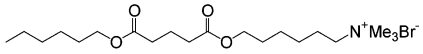
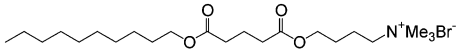
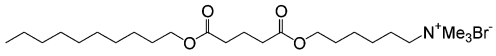
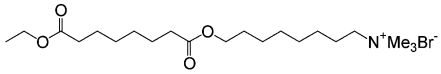
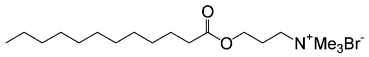
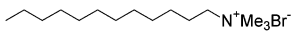
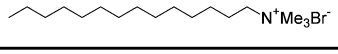
Abstract: This paper addresses a question not yet posed systematically in surfactant chemistry: How do the colloidal properties of surfactants respond to insertion of non-hydrocarbon functionalities (i.e., ester groups) within chains that are normally entirely hydrocarbon? In answering this question, two classes of such chain-modified surfactants were discovered. One class forms only small aggregates with noncooperative self-assembly, low foaming, high areas of occupancy at the air/water interface, and weak solid-adsorption and solubilization properties. The other class is much more normal with regard to these properties and, in fact, can even exceed conventional surfactants in mesitylene solubilization. Differences between the two categories of chain-modified surfactants originate from the degree of segmentation of the hydrocarbon and, in particular, upon the location of the longest segment. Segmented hydrophobicity, having in principle a "hydrophobic potential" similar to that of a contiguous hydrophobicity of equal length, can induce aggregation but, concurrently, alters the mode of assembly into films and micelles.

Introduction

Occasionally in the literature one finds examples of people addressing an important question in colloid chemistry: How does the presence of non-hydrocarbon functional groups within a surfactant's chain affect the self-assembly process and the properties of the resulting aggregates? One of the first and most interesting papers confronting this issue was penned by Muller and Birkhahn in 1967.[1] These chemists deduced from solvent-sensitive ^{19}F NMR signals that the terminal $-CF_3$ group of micellar $CF_3(CH_2)_nCOONa$ experiences a polarity midway between water and hydrocarbon. We ourselves, while examining monomolecular films of 10-hydroxystearic acid, found that the hydroxyl and polar headgroup maintain contact with an aqueous subphase while the intervening chains form "loops" above it.[2] Despite such work, there has been to our knowledge no systematic study of what might be termed "interrupted" hydrophobicity. How, for example, will the relative location of two semipolar groups within a hydrocarbon chain affect its propensity to assemble? In this manuscript, we now describe synthetic pathways to several cationic surfactants bearing ester-modified chains (Table 1). More pertinently, we discuss the physical chemistry of fundamentally new surfactant systems that organic synthesis has now placed at our disposal.[3]

The decision to incorporate ester groups into the surfactant chains needs explanation. Conventional surfactants consist of two sections: a hydrophilic headgroup and a hydrophobic tail. The headgroup serves one main purpose: to promote solubility of the hydrophobic tail in water. Once this happens, the tails self-assemble into a micelle that can then solubilize or disperse insolubles in water. Solubilization/dispersal is by far the most important property of surfactants;[4−6] huge industries rely on the concept. Now most organic solubilizates reside in the hydrophobic portion of the micelles (sometimes near the micelle surface, sometimes in the interior). Yet a purely hydrocarbon

Table 1. Structure of Ester-Modified Surfactants **A**−**F** and Two Conventional Surfactants, DTAB and TTAB

Label	*#CH$_2$'s*	*Structure*
A	12	
B	14	
C	16	
D	18	
E	15	
F	13	
DTAB	11	
TTAB	13	

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(2) Menger, F. M.; Richardson, S. D.; Wood, M. G., Jr.; Sherrod, M. J. *Langmuir* **1989**, *5*, 833.
(3) For an excellent review of new surfactants, consult: Chevalier, Y. *Curr. Opin. Colloid Interface Sci.* **2002**, *7*, 3.
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(6) Almgren, M.; Grieser, F.; Thomas, J. K. *J. Am. Chem. Soc.* **1979**, *101*, 279.

environment would not be expected to have a particularly great capacity for dissolving modestly polar organics. Hexane, for example, is usually a poor solvent for organics with even a single polar group. If, however, a surfactant chain could be made somewhat less hydrocarbon-like, but (importantly!) not to such an extent as to prevent self-assembly, then one might obtain a much more potent solubilizing entity. In the same way that ethyl acetate is a better solvent than hexane, the presence of two ester groups in a surfactant (or 100 ester groups per 50-surfactant micelle) might enhance the partitioning of organic guests from the bulk water phase into the micelles. Such was the reasoning behind the design of the compounds in Table 1.

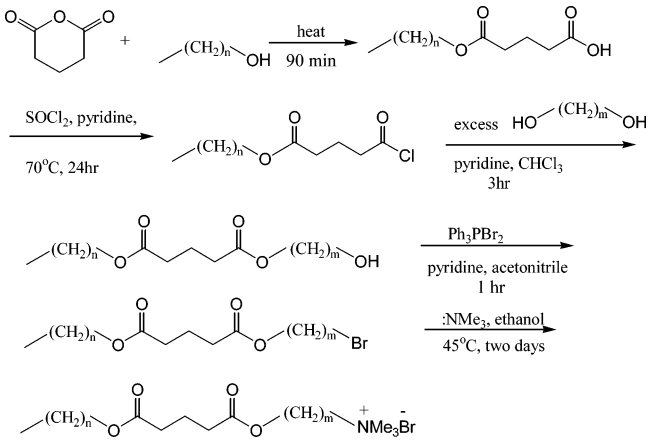
No more than two ester groups were inserted into the chains (Table 1) as a conservative compromise between increasing the micelle's interior polarity as much as possible while not preventing the micellization process. It was felt at the outset that the esters would not prevent micellization if the surfactants were also provided with sufficient hydrocarbon. The poor miscibility of ethyl acetate in water supports this expectation, as does the Handbook of Surfactant Analysis which refers to esters as lipophilic.[7] On a more quantitative footing, the Hansch π-parameters (based on octanol/water partition coefficients) have the following values: $Et_2O = 7.8$; EtOAc = 9.1; $CHCl_3 = 9.5$; and MeOH = 14.2.[8] We concluded from such data that micelles should be able to tolerate a modest number of ester groups and that, when they do, the properties of the micelles should likely be altered.

There was a second and more fundamental reason for examining ester-modified surfactants. This had to do with the concept of hydrophobicity, a concept that has been well-developed over the years owing to the efforts of (among others) Hildebrand,[9] Harkins,[10] Tanford,[11] Kauzmann,[12] Frank,[13] Némethy,[14] Scheraga,[15] Ben-Haim,[16] Rekker,[17] and Engberts.[18] In brief, contact between two hydrocarbon chains in aqueous systems releases "structured" water (an entropically favorable process), and, as a consequence, the hydrocarbons experience a stronger interaction energy in water than would be expected solely from van der Waals forces in free space. This is the hydrophobic effect. This is why surfactants form micelles in water, and lipids assemble into membranes.

Past work notwithstanding, there exist substantial gaps in our understanding of hydrophobic association. In particular, it is not known if hydrophobic association among discrete hydrophobic regions is additive. Will, for example, a chain that is 12 methylenes in length provide a greater hydrophobic driving force than a chain of equal length but separated into three sets of four methylenes? Asked in another way consistent with this paper's title, "How do contiguous and segmented associations compare?"

Engberts and co-workers have carried out kinetic studies relevant to our concerns.[19,20] They studied the effect of short-chain sulfates and ammonium salts on the neutral hydrolysis of 1-benzoyl-1,2,4-triazole. The cosolutes bind to the triazole substrate and inhibit its hydrolysis. The key point is that the first two or three CH_2 groups near the ionic groups of the cosolutes do not seem to contribute substantially to the cosolute/substrate binding. It is as if the sulfate and ammonium groups shield the proximal methylenes and impair their availability for hydrophobic association. Of course, our ester group is less polar than the ionic groups, and its shielding would be expected to be less extensive.

Scheme 1. Synthetic Route to Surfactants **A**−**D**



In summary, this work was carried out to alter and, possibly, improve surfactant properties. (Certainly, the presence of ester groups would promote surfactant biodegradability!) Also, on a more basic level, we hoped to learn something about "interrupted" hydrophobic association.

Synthesis

As seen in Table 1, we studied five new diester-loaded surfactants (**A**−**E**) plus a monoester (**F**) and, for comparison purposes, two conventional surfactants, DTAB and TTAB. The synthetic route to **A**−**D** is shown in Scheme 1, the route to **E** is shown in Scheme 2, and the route to **F** is shown in Scheme 3. As detailed in the Experimental Section, all new surfactants were chromatographically pure and characterized by ^1H and ^{13}C NMR, HRMS, and EA. Table 1 also lists the total number of methylenes in the eight compounds as a qualitative measure of their "hydrophobic potential".

Results and Discussion

Our physical-chemical data are largely summarized in Table 2. Let us begin with the critical micelle concentration (cmc) values listed in column 2 of this table. Cmc's, the most representative micelle descriptor, were obtained from the breaks in the surface tension versus concentration plots, two examples of which are shown in Figure 1. As a rough rule of thumb, cmc values decrease by a factor of 4 as the surfactant chain increases by two carbons.[21] In this light, the similarity in cmc values for **F** and TTAB (both with 13 methylenes and with cmc's of 4.6 and 3.3 mM, respectively) would suggest only a slight effect

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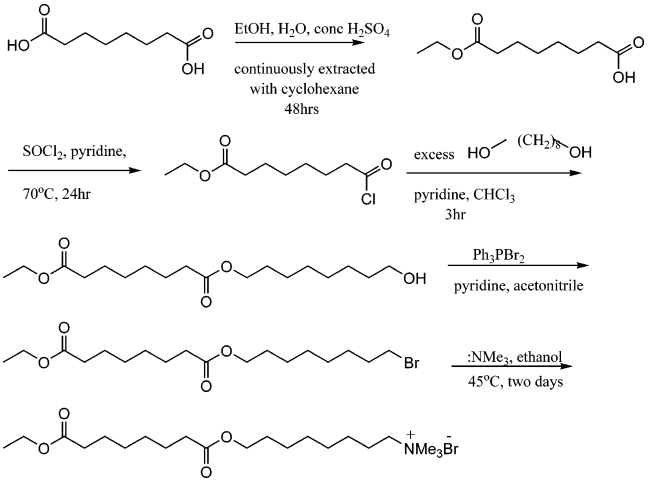
Scheme 2. Synthetic Route to Surfactant **E**



Scheme 3. Synthetic Route to Surfactant **F**

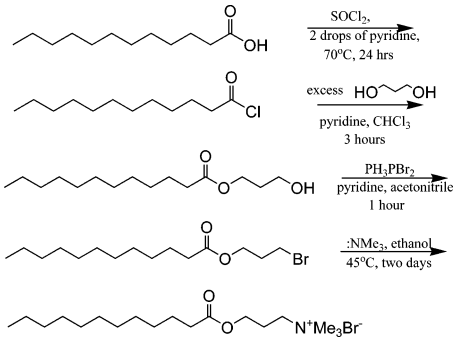


Table 2. Colloidal Properties of Ester-Modified Surfactants and Two Conventional Surfactants

surfactant	cmc,[a] mM	area, Å^2	foam vol., mL	TMS,[b] mM	mesitylene,[b] mM
A	2.4	81	0.01	0	1.7
B	2.5	123	0.48	0.026	5.3
C	2.2	75	2.5	1.2	38
D	1.4	75	3.2	5.2	93
E	1.0	334	0.04	0	0
F	4.6	54	3.5	5.4	27
DTAB	13.3	64	1.9	0.51	13
TTAB	3.3	52	3.3	7.9	36

[a] The cmc values for **A**, **B**, and **E** are approximate; see Figure 1A. [b] Refers to the amount of TMS or mesitylene solubilized by the surfactant (see text).

of **F**'s lone ester group on the tendency to assemble. Yet unfortunately things are not quite so straightforward. Differences in cmc among **A**−**E** are small (covering a range of only 1.0−2.5 mM) despite large differences in total chain-length (12 CH_2's for **A** but 18 CH_2's for **D**). Part of the difficulty in explaining these data relates to the fact that the cmc is a multi-faceted thermodynamic parameter reflecting both the solvation properties of the monomer and the packing constraints within a spherical micelle. Importantly, the cmc reveals only the concentration at which a surfactant self-assembles, and not the size and morphology of the micelles thus formed. As a consequence, two surfactants with an identical cmc might have, on one hand, a large conventional aggregation number (i.e., 50−100), while, on the other hand, they might have a small aggregation number (i.e., 5−10) of loosely assembled molecules (only marginally deserving of the name "micelle").

The surface tension data such as in Figure 1 show that, in fact, morphology differences among the surfactants are playing an important role. Only **C**, **D**, and **F** display surface tension versus concentration plots that level off sharply into horizontal lines as happens when there is a cooperative assembly into large micelles. Surfactants **A**, **B**, and **E**, on the other hand, show a steady post-cmc decline in surface tension as would be expected from a less precipitous assembly into small aggregates. Dynamic light scattering, using a 10 mW laser, confirms the above conclusions: micelles of **C**, **D**, and **F** in 0.1 M NaCl have 3−4 nm hydrodynamic diameters, whereas **A**, **B**, and **E** aggregates fall below the 3 nm resolution of the instrument. As a consequence, the properties of the **A**, **B**, **E** set are not easily compared to those of the **C**, **D**, **F** set. For example, **D** (with 18 CH_2's) might have been expected to have a much lower cmc than **A** (with only 12 CH_2's), yet the cmc's are similar. Additional physical-chemical data, to be revealed presently, consistently reinforce this same dichotomy among the two sets of surfactants.

The presence of two sets of micelle morphologies complicates answering the interesting question: "Is the ester group hydrophobic or hydrophilic?" With surfactant **A**, **B**, and **E**, the ester groups have a rather minor effect upon the cmc. For example, **E**, with a total of 15 CH_2's, has a cmc of 1.0 mM, which is only slightly larger than the cmc of 0.9 mM for the corresponding surfactant, cetyltrimethylammonium bromide, with 15 CH_2's and no esters.[22] Apparently, when a micelle is small, the ester linkages play little role in the micellization. Association among relatively short hydrocarbon segments presumably forms "wet" aggregates in which ester group hydration, such as it is, is not impaired. Thus, the esters do not perturb the micelle-forming equilibrium.

The situation is different with the larger, more conventional micelles formed in **C**, **D**, and **F**. Here, the ester groups definitely impair micellization as reflected by the cmc values. Thus, **D** with 18 CH_2's has a cmc that is 14-fold higher than its hydrocarbon analogue where esters are absent.[22] Undoubtedly, ester polarity and/or packing constraints, imposed in part by the esters' *s-trans* O−CO linkage, contribute to the reduced tendency for ester-endowed chains to assemble into compact apolar units. When, however, the three surfactants do reach their critical concentrations, the resulting micelles are rather normal.

Differences in packing constraints between the two groups of surfactants, **A**/**B**/**E** and **C**/**D**/**F**, are seen from the area-per-molecule occupied at the air/water interface (derived in the standard way from pre-cmc tensiometric data and the Gibbs adsorption isotherm).[23] It is seen from Table 2, column 3, that **A**, **B**, and (especially) **E** have inordinately large molecular areas. For example, **E** has an area of roughly 334 Å^2/molecule as compared to 52 Å^2/molecule for TTAB with its all-hydrocarbon chain. The large areas for **A**/**B**/**E** reveal the reluctance of these three surfactants to self-assemble into a monomolecular film just as they are reluctant to self-assemble into large micelles.

It behooves us to explain why **A**/**B**/**E** form small and presumably loose aggregates, whereas micelles from **C**/**D**/**F** are

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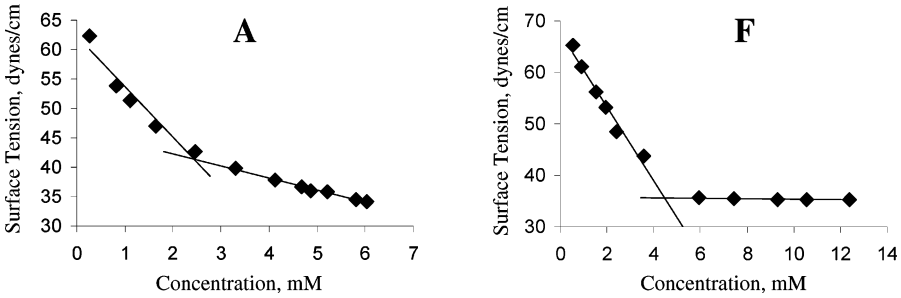

Figure 1. Surface tensiometry plots of ester-modified surfactants **A** and **F**.

more normal in constitution. Inspection of the structures in Table 1 provides a rationale. Thus, the longest contiguous hydrocarbon segments in **A**, **B**, and **E** are 6, 6, and 8 carbons in length, respectively. By contrast, the values for **C**, **D**, and **F** are 10, 10, and 11, respectively. Moreover, these latter three segments are all terminal. It seems critical, therefore, that a long contiguous stretch of terminal carbons is necessary for formation of conventional micelles (at least when ester groups constitute the intervening functionalities). A comparison of **C** and **E** drives this point home. **C** has a total of 16 CH_2's with a contiguous terminal segment of 10 carbons. **E** has a similar total number of CH_2's (15), but its longest segment is only 8 carbons, and the segment is not terminal. The main conclusion is, therefore, that segment length and location play an important role in micelle formation, not so much in the cmc as in micelle morphology. Stated in another way, a segmented hydrophobicity, having in principle a "hydrophobic" potential similar to that of a contiguous hydrophobicity of equal length, can certainly induce aggregation. Yet at the same time, packing constraints imparted by the ester spacers alter the mode of assembly into films and micelles.

Having two categories of related surfactants on hand led us to wonder about their differences in various colloidal properties including foamability. Foamability experiments were carried out by inverting and uprighting 10 times a 50 mL buret containing 5 mL of surfactant solution (at concentrations 3 times greater than its cmc), and then measuring the volume of the resulting foam.[24] The data are recorded in Table 2, column 4. As seen, **A**, **B**, and **E** are capable of sustaining only low volumes of foam (0.01−0.48 mL) in contrast to **C**, **D**, and **F** and the two controls (1.9−3.5 mL). Once again, the data support the notion that **A**, **B**, and **E**, with their short terminal segments, have difficulty aligning their chains at the air/water interface so as to stabilize a film. An interesting comparison exists among **A**, **B**, and **E**: Although all have low foamability, **B** is by far the best of the three (0.48 mL as compared to 0.01 and 0.04 mL). An explanation (tentative as we would need additional compounds that at the moment have not been synthesized) is based on the carbon-lengths of the initial and terminal segments of the three surfactants: **A** (4, 6), **B** (6, 6), and **E** (8, 2). In **A**, the initial segment is short, while in **E** the even more important terminal segment is only two carbons and contributes little to the hydrophobic overlap. **B** is an improvement over **A** and **E** in both respects. If this is correct, then we can predict, for example, that a (2, 8) would likely emulate **B**'s foamability.

Reverse-phase HPLC was used to qualitatively measure the solid-adsorption properties of the eight surfactants in Table 1.

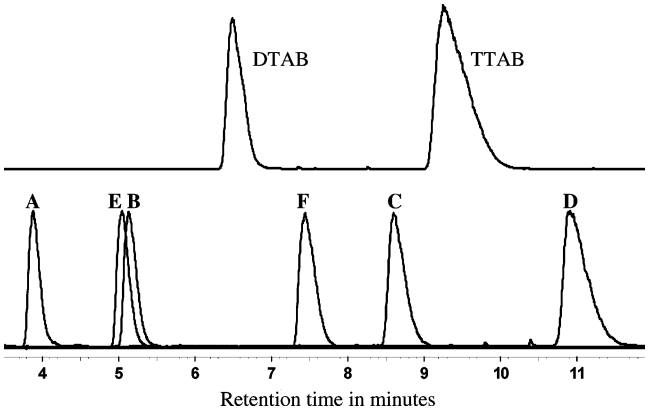

Figure 2. HPLC traces of ester-modified surfactants **A**−**F** as well as two conventional surfactants, DTAB and TTAB, on a reverse-phase column.

Samples (1.0 mg/mL) were injected into an Alltech Surfactant/R column containing a 7 μm polydivinylbenzene-based resin. A solvent system was comprised of a 60% 10 mM HCl/40% CH_3CN mixture for the first 5 min followed by a 30% 10 mM HCl/70% CH_3CN mixture for the remainder of the experiment. Nitrogen flow at ambient temperature (1.0 mL/min) was used for all runs. As seen in Figure 2, surfactants **A**, **B**, and **E** have shorter retention times on the hydrophobic surface than does DTAB, whereas surfactants **C**, **D**, and **F** have longer retention times. These results are consistent with the large adsorption areas for **A**, **B**, and **E** in Table 2. As compared to surfactants **C**, **D**, and **F**, surfactants **A**, **B**, and **E** bind rather ineffectively to each other and to hydrophobic surfaces.

In the introduction of this paper, we mentioned the industrial importance of solubilization by surfactants. It was, therefore, natural to investigate the solubilization properties of our new surfactants. A priori, we could not predict how the ester-substituted chains would affect solubilization. For one thing, it was not clear whether solubilization is promoted by solubilizate/monomer interactions or by solubilizate/micelle adsorption (the latter being favored at concentrations well above the cmc values). At least two possibilities exist if micelles dominate the solubilization mechanism: (a) The esters might increase the polarity of the micelle interior and thus enhance solubilization of moderately polar organics (much as ethyl acetate is a better chromatographic solvent than hexane). (b) The *s-transoid* esters might impair chain assembly into a micelle (and, as discussed, we think this happens with **A**, **B**, and **E**), leading to loose aggregates that are less effective solubilizers. Because the solubilization properties could well be solubilizate-dependent, we examined three of them: tetramethylsilane (TMS, a lipophilic compound with no dipole moment), mesitylene (1,3,5-

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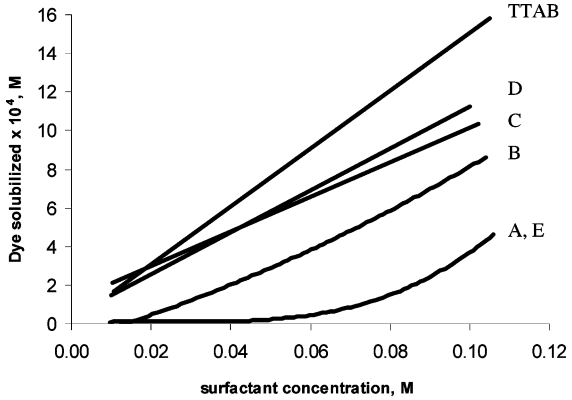
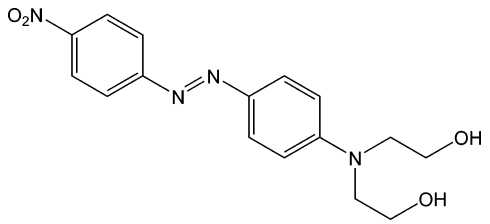


Figure 3. Disperse Red 19 solubilization in water as a function of surfactant concentration. Six data points were used to construct each line, which is presented as a visual guide. **A** and **E** were within experimental error of one another, so only one line is shown.

trimethylbenzene, an aromatic), and Disperse Red 19 (a polar dye, drawn below).



Excess amounts of TMS or mesitylene (both liquids) were vortexed with 40 mM surfactant in D_2O followed by ^1H NMR analysis of the solubilized material in the D_2O after the layers had separated. The results for TMS and mesitylene are given in columns 5 and 6 of Table 2, respectively. Note that 40 mM of surfactant lies appreciably above all of the surfactants' cmc values, so that we are dealing here primarily with micellar behavior.

Surfactants **A**, **B**, and **E** are seen to be poor solubilizers of both TMS and mesitylene. For example, **A** and **B** solubilize 1.7 and 5.3 mM mesitylene, respectively, as compared to 13 and 36 mM for DTAB and TTAB, respectively. Perhaps not surprisingly, **A** and **B**, with their small, loose, and no doubt "wet" aggregates, adsorb "little" nonpolar solubilizate. Remarkably, surfactant **E** (despite having a total of 15 CH_2's) failed to solubilize any TMS or mesitylene at all. Once again, the terminal tail, only two carbons long in **E**, reveals its importance.

On the other hand, surfactants **C**, **D**, and **F** are reasonably good solubilizers. Thus, **C** and **D** solubilize 38 and 93 mM mesitylene, respectively, as compared to only 13 and 36 mM for DTAB and TTAB, respectively. Surfactant **D** solubilizes 10 times more TMS than does DTAB. These comparisons are, of course, not totally fair because **C** and **D** possess a greater number of carbons than do DTAB and TTAB. Probably, the most straightforward comparison comes from **F** versus TTAB, both of which have 13 CH_2's. In this case, **F** has only a slightly lower solubilization power for TMS and mesitylene than does TTAB, indicating that a single ester group neither substantially assists nor detracts from micellar adsorption.

Figure 3 plots the concentration of solubilized Disperse Red 19 (determined spetrophotometrically) versus surfactant concentration for the five diester compounds in Table 2. Only the plots for **A**, **B**, and **E** are nonlinear (perhaps reflecting aggregate growth and enhanced solubilization at higher concentrations). Among the generalizations we can state: (a) Total carbon content is not always an accurate predictor of solubilization power (**B** with 14 CH_2's is better than **E** with 15 CH_2's; **C** and **D** are similar, although **D** has 2 more CH_2's). (b) The length of the terminal chain is critical (**C** and **D** with 10 terminal carbons are the best solubilizers; **E**, with 2 terminal carbons, is no better than **A**, with 6 terminal carbons, although the former has more total hydrocarbons. (c) All new surfactants are less powerful solubilizers than TTAB, suggesting that the ester groups' potential solubilizing ability for polar compounds is overridden by unfavorable perturbations in the micellar structure.

In summary, we have examined a variety of colloidal properties of six new surfactants bearing one or more ester groups within their chains. Systematic studies of chain-modified surfactants are rare,[25] and even this brief entry into the field has revealed useful structural relationships. Modification of micelle chains (and lipid chains in bilayer membranes) clearly merits further synthetic and physicochemical attention.

Experimental Section

Materials. Solvents used in this synthesis were reagent grade and dried over 4 Å molecular sieves. Reagents were purchased from Aldrich or Fluka and used without additional purification.

Methods. ^1H NMR and ^{13}C NMR spectra were taken on either a Varian INOVA 400 mHz (100 mHz for ^{13}C) or a Mercury 300 mHz (75 mHz for ^{13}C) instrument. Mass spectra experiments were completed by the Emory University Mass Spectrometry Center, and Atlantic Microlabs in Norcross, GA performed all elemental analyses. HPLC experiments were completed on a Shimadzu LC-10AT VP instrument, and the solubilization of Disperse Red 19 was measured on a Varian DMS 300 UV−visible spectrophotometer at $\lambda_{max} = 494$ nm.

Syntheses. General Procedure for Compound 1.[26,27] **5-(Hexyloxy)-5 Oxopentanoic Acid (1, *n* = 5).** A mixture of glutaric anhydride (10.73 g, 94.0 mmol, 1 equiv) and hexanol (11.42 g, 111.8 mmol, 1.2 equiv) was heated and stirred in a 90 °C oil bath until the mixture became homogeneous (1 h). After homogeneity was reached, the reaction temperature was raised to 105 °C for 30 min. Once the reaction had cooled, 50 mL of a saturated sodium bicarbonate solution was added to dissolve the product. The excess hexanol in solution was extracted with 3 × 50 mL portions of ether. Next, the pH of the aqueous layer was lowered to 3 with dilute HCl, followed by an extraction of the desired product with 3 × 50 mL portions of ether. The ether layer was then dried over $MgSO_4$, and the solvent was evaporated under reduced pressure to yield a yellow oil. Yield: 19.77 g (97.4%). ^1H NMR (300 mHz, $CDCl_3$): δ 4.05 (t, 2H), 2.42 (t, 2H), 2.38 (t, 2H), 1.94 (m, 2H), 1.60 (m, 2H), 1.28 (m, 6H), 0.87 (t, 3H). ^{13}C NMR (75 mHz, $CDCl_3$): δ 179.5, 173.2, 64.9, 33.4, 33.2, 31.6, 28.7, 25.7, 22.7, 20.0, 14.2. Mass spectra: M + Li 223.1522 amu, found 223.1512 amu.

5-(Decyloxy)-5-oxopentanoic Acid (1, *n* = 9). Yield = 85%, white solid. ^1H NMR (400 mHz, d_6-DMSO): δ 4.05 (t, 2H), 2.41 (m, 4H), 1.94 (m, 2H), 1.60 (m, 2H), 1.25 (m, 14H), 0.859 (t, 3H). ^{13}C NMR (100 mHz, d_6-DMSO): δ 179.6, 173.6, 65.26, 33.71, 33.52, 32.38, 30.01 (2 C's), 29.79, 29.74, 29.08, 26.40, 23.17, 20.33, 14.59.

General Procedure for Compounds 2, 7, 11.[26,27] **Hexyl 5-Chloro-5-oxopentanoate (2, *n* = 5).** Compound **1** (*n* = 5) (17.11 g, 79.2 mmol, 1 equiv) and 2 small drops of dry pyridine were stirred in a round-bottom flask with a condenser and drying tube attached. An excess (11.99 g, 100.1 mmol, 1.3 equiv) of thionyl chloride was added to the

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reaction, and the mixture was heated in an oil bath at 70 °C for 24 h. Excess thionyl chloride was evaporated under reduced pressure to produce 13.28 g (71% yield) of a reddish brown liquid. IR (neat, cm^{-1}): 1804, 1733.

Decyl 5-Chloro-5-oxopentanoate (2, $n = 9$). Reddish brown liquid, 94.6% yield (immediately carried to next reaction without additional characterization).

Ethyl 8-Chloro-8-oxooctanoate (7). Yield = 97.3%, reddish brown liquid (immediately carried to next reaction without additional characterization).

Dodecanoyl Chloride (11). Yield = 96%, opaque colorless liquid (immediately carried to next reaction without additional characterization).

General Procedure for Compounds 3, 8, 12.[28,29] **Hexyl 4-Hydroxybutylpentanedioate (3, $n = 5$, $m = 4$).** Compound **2** ($n = 5$) (13.28 g, 56.5 mmol, 1 equiv) was diluted in 50 mL of dry $CHCl_3$ and placed in a separatory funnel. Butane diol (50.86 g, 564.4 mmol, 10 equiv) and 20 mL of dry pyridine were placed in a round-bottom flask and put on stir at 0 °C. After the diol mixture was cooled to 0 °C, compound **2** ($n = 5$) in the separatory funnel was slowly dripped into the round-bottom flask. The reaction was covered with a drying tube and allowed to sit on ice. After 15 min, the reaction was removed from ice and stirred at room temperature for 3−4 h. Once the reaction completed, the mixture was poured into 20 mL of H_2O and extracted with $CHCl_3$ (3 × 50 mL). The chloroform layer was concentrated down to 75 mL, and then washed with several 50 mL portions of 0.1 N HCl to remove excess pyridine. After the pyridine was removed, the chloroform layer was washed with 2 × 50 mL portions of distilled water and dried over $MgSO_4$. A silica column was then used to separate the desired alcohol and the disubstituted product using a 1:1 ethyl acetate/hexane solvent system. Ten milliliter fractions were collected, and the contents were identified using a Phosphomolybdic acid TLC stain. Product fractions were collected, and the solvent was then evaporated under reduced pressure to yield a light brown oil. Yield: 11.73 g (71.7%). ^{1}H NMR (300 mHz, $CDCl_3$): δ 4.06 (t, 2H), 4.01 (t, 2H), 3.61 (t, 2H), 2.32 (t, 2H), 2.31 (t, 2H), 2.1 (br s, 1H) 1.89 (m, 2H), 1.75−1.5 (m, 6H), 1.25 (m, 6H), 0.83 (t, 3H). ^{13}C NMR (75 mHz, $CDCl_3$): δ 172.8, 172.7, 64.4, 64.0, 62.0, 33.1 (2C), 31.1, 28.8, 28.3, 25.3, 24.8, 22.2, 19.9, 13.7. Mass spectra: M + Li 295.2097 amu, found 295.2090 amu.

Hexyl 6-Hydroxylhexylpentanedioate (3, $n = 5$, $m = 6$). Yield = 83.9%, light brown oil. ^{1}H NMR (300 mHz, $CDCl_3$): δ 3.98 (dt, 4H), 3.54 (t, 2H), 2.29 (dt, 4H), 1.86 (m, 2H), 1.53 (m, 6H), 1.30−1.22 (m, 10H), 0.804 (t, 3H). ^{13}C NMR (75 mHz, $CDCl_3$): δ 173.09, 173.08, 64.63, 64.46, 62.53, 33.34, 32.53, 31.42, 29.37, 28.57, 28.49, 25.74, 25.57, 25.42, 22.52, 20.21, 13.99.

Decyl 4-Hydroxybutylpentanedioate (3, $n = 9$, $m = 4$). Yield = 75.8%, light brown oil. ^{1}H NMR (400 mHz, $CDCl_3$): δ 4.08 (t, 2H), 4.03, (t, 2H), 3.64 (t, 2H), 2.34 (dt, 4H), 1.92 (m, 2H), 1.68 (m, 2H), 1.58 (m, 2H), 1.23 (m, 16H), 0.85 (t, 3H). Mass spectra: theory $(M + H)^+$ 345.2641 amu, observed 345.2653 amu.

Decyl 6-Hydroxyhexylpentanedioate (3, $n = 9$, $m = 6$). Yield = 55.1%, light brown oil. ^{1}H NMR (400 mHz, $CDCl_3$): δ 4.02 (m, 4H), 3.58 (t, 2H), 2.32 (dt, 4H), 1.89 (m, 2H), 1.57 (m, 6H), 1.34−1.21 (m, 18H), 0.829 (t, 3H). ^{13}C NMR (100 mHz, $CDCl_3$): δ 173.21, 173.18, 64.76, 64.55, 62.72, 33.43, 32.66, 31.98, 29.62, 29.40, 29.34 (2C), 28.70 (2C), 26.00, 25.83, 25.69, 25.50, 22.77, 20.29, 14.21. Mass spec. theory $(M + H)^+$ 373.2954 amu, observed 373.2935 amu.

Ethyl 8-Hydroxyoctylsuberate (8). Yield = 56.6%, light brown oil. ^{1}H NMR (400 mHz, d_6-DMSO) δ 4.02 (t, 2H), 3.98 (t, 2H), 3.37 (t, 2H), 2.26 (dt, 4H), 1.50−1.252 (m, 20H), 1.16 (t, 3H). ^{13}C NMR (100 mHz, d_6-DMSO): δ 172.83, 172.78, 63.61, 60.72, 59.62, 33.40, 32.57, 29.06, 28.88, 28.54, 28.08, 25.51, 25.45, 25.39, 25.32, 24.31, 24.27, 14.09.

Dodecanoic Acid 3-Hydroxypropyl Ester (12). Yield = 60.3%, off-white solid. ^{1}H NMR (400 mHz, $CDCl_3$): δ 4.207 (t, 2H), 3.659 (t, 2H), 2.282 (t, 2H), 1.84, (m, 2H) 1.588 (m, 2H), 1.229 (m, 16H), 0.848 (t, 3H). ^{13}C NMR (100 mHz, $CDCl_3$): δ 174.6, 61.3, 59.3, 34.5, 32.1, 31.9, 29.8 (2C), 29.6, 29.5, 29.4, 29.3, 25.2, 22.9, 14.3.

General Procedure for Compounds 4, 9, 13.[30,31] **4-Bromobutyl Hexylpentanedioate (4, $n = 5$, $m = 4$).** A solution of compound **3** ($n = 5$, $m = 4$) (11.51 g, 39.9 mmol, 1 equiv), pyridine (5.55 g, 70.2 mmol, 1.7 equiv), and 50 mL of acetonitrile was stirred at 0 °C. After 10 min, 21.79 g (51.62 mmol, 1.3 equiv) of solid triphenylphosphine dibromide was added to the mixture. The reaction was removed from ice, covered with a drying tube, and stirred at room temperature for 1 h. After 1 h, the solvents were stripped, and the crude product was triturated in hexanes at reflux for 3 h. Hexanes were collected by vacuum filtration, and the solvent was evaporated under reduced pressure. The resulting product was filtered through a 2-in. pad of silica and rinsed with 200 mL of a 10% ether/pentane solution. After the solvents were stripped, 9.05 g (64.7%) of yellow oil emerged. ^{1}H NMR (400 mHz, $CDCl_3$): δ 4.09 (t, 2H), 4.05 (t, 2H), 3.42 (t, 2H), 2.36 (t, 2H), 2.35 (m, 2H), 1.93 (m, 2H), 1.80 (m, 2H), 1.60 (m, 2H), 1.29 (m, 6H), 1.26 (t, 2H), 0.87 (m, 3H). ^{13}C NMR (100 mHz, $CDCl_3$): δ 178.3, 173.2, 64.8, 63.6, 33.5, 33.4, 33.2, 31.6, 29.4, 28.7, 27.4, 25.7, 22.7, 20.3, 14.2. Mass spectra: $(M + H)^+$ (^{81}Br) 353.1150 amu, found 353.1153 amu, $(M + H)^+$ (^{79}Br) 351.1171 amu, found 351.1164 amu.

6-Bromohexyl Hexylpentanedioate (4, $n = 5$, $m = 6$). Yield = 66.4%, yellow oil. ^{1}H NMR (400 mHz, $CDCl_3$): δ 4.06 (m, 4H), 3.39 (t, 2H), 2.36 (dt, 4H), 1.94 (m, 2H), 1.86 (m, 2H), 1.61 (m, 4H), 1.46 (m, 2H), 1.36−1.28 (m, 8H), 0.878 (m, 3H). ^{13}C NMR (100 mHz, $CDCl_3$): δ 173.22, 173.21, 64.82, 64.49, 33.88, 33.54, 32.78, 31.61, 28.76, 28.75, 28.63, 27.96, 25.76, 25.34, 22.72, 20.39, 14.19.

6-Bromohexyl Decylpentanedioate (4, $n = 9$, $m = 6$). Yield = 63.7%, yellow oil. ^{1}H NMR (400 mHz, $CDCl_3$): δ 4.04 (dt, 4H), 3.38 (t, 2H), 2.34 (dt, 4H), 1.92 (m, 2H), 1.59 (m, 6H), 1.23 (m, 18H), 0.848 (m, 3H). Mass spectra: theory $(M + H)^+$ 435.2110 amu, observed 435.2114 amu.

8-Bromooctyl Ethylsuberate (9). Yield = 62.7%, yellow oil. ^{1}H NMR (400 mHz, $CDCl_3$): δ 4.09 (t, 2H), 4.03 (t, 2H), 3.38 (t, 2H), 2.26 (dt, 4H), 1.83 (m, 4H), 1.60 (m, 4H), 1.41−1.31 (m, 12H), 1.23 (t, 3H). ^{13}C NMR (100 mHz, $CDCl_3$): δ 173.95, 173.86, 64.47, 60.33, 34.42 (2C's), 34.08, 32.89, 29.19 (2C's), 28.91, 28.78, 28.73, 28.2 (2 C's), 25.97, 24.92, 14.42.

Dodecanoic Acid 3-Bromopropyl Ester (13). Yield = 97%, yellow oil. ^{1}H NMR (400 mHz, $CDCl_3$): δ 4.188 (t, 2H), 3.444 (t, 2H), 2.285 (t, 2H), 2.157 (m, 2H), 1.597 (m, 2H), 1.265 (m, 16H), 0.859 (t, 3H).

General Procedure for Compounds 5, 10.[32] **Surfactant A (5, $n = 5$, $m = 4$).** First, 8.8406 g (25.3 mmol, 1 equiv) of compound **4** ($n = 5$, $m = 4$) and 25 mL of ethanol were placed in a round-bottom flask and magnetically stirred in a 45 °C oil bath. The solution was treated with 5.5392 g (30.9 mmol, 1.2 equiv) of 33% trimethylamine in ethanol. A drying tube covered the flask, and the reaction continued for 2 days at 45 °C. Upon completion, the reaction was removed from heat and the solvent was stripped. Ether (50 mL) was added to the crude product followed by an extraction of the desired product with 3 × 50 mL portions of water. The water was removed by sublimation to yield 4.54 g (44% yield) of a flakey white powder. ^{1}H NMR (300 mHz, D_2O): δ 4.16 (t, 2H), 4.09 (t, 2H), 3.42 (m, 2H), 3.15 (s, 9H), 2.45 (m, 2H), 2.42 (m, 2H), 1.91−1.63 (m, 8H), 1.31 (m, 6H), 0.88 (t, 3H). ^{13}C NMR (75 mHz, D_2O): δ 175.3 (2C's), 65.3, 64.3, 33.2, 33.1, 31.2, 28.2, 25.3, 25.0, 22.3, 20.0, 19.5, 13.6. Mass spec. theory $(M - Br)^+$

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330.2644 amu, found 330.2628 amu. Elemental analysis: theory (surfactant **A** + $1H_2O$) 50.56% C, 8.96% H, 3.28% N; found 50.25% C, 8.74% H, 3.29% N.

Surfactant B (5, *n* = 5, *m* = 6). Yield = 43%, flakey white powder. ^{1}H NMR (400 mHz, d_6-DMSO): δ 4.01 (t, 2H), 3.996 (t, 2H), 3.33 (m, 2H), 3.046 (s, 9H), 2.35 (t, 2H), 2.31 (t, 2H), 1.8−1.5 (m, 8H), 1.26 (m, 10H), 0.856 (m, 3H). ^{13}C NMR (100 mHz, d_6-DMSO): δ 172.48, 172.46, 65.15, 63.80, 63.64, 52.10, 32.53 (2C), 30.82, 28.05, 27.82, 25.34, 25.00, 24.87, 21.98, 21.92, 19.93, 13.86. Mass spec. theory $(M - Br)^+$ 358.2957 amu, found 358.2968 amu. Elemental analysis: theory (surfactant **B** + $1H_2O$) 52.72% C, 9.30% H, 3.08% N; found 52.60% C, 9.35% H, 3.23% N.

Surfactant C (5, *n* = 9, *m* = 4). ^{1}H NMR (300 mHz, D_2O): δ 4.13 (t, 2H), 4.04 (t, 2H), 3.36 (m, 2H), 3.13 (s, 9H), 2.43 (t, 4H), 1.87 (m, 4H), 1.84 (m, 2H), 1.72 (m, 2H), 1.26 (m, 14H), 0.85 (m, 3H). ^{13}C (100 mHz, d_6-DMSO): 172.42, 172.39, 64.6, 63.76, 63.03, 52.04, 32.52, 32.48, 31.26, 28.9 (2 C's), 28.66, 28.62, 28.08, 25.32, 24.99, 22.07, 19.84, 18.92, 13.89. Mass spec. theory $(M - Br)^+$ 386.3270 amu, observed 386.7836 amu. Elemental analysis: theory (surfactant **C** + $1H_2O$) 54.63% C, 9.59% H, 2.90% N; found 54.47% C, 9.56% H, 2.85% N.

Surfactant D (5, *n* = 9, *m* = 6). Yield = 54.7%, fluffy white powder. ^{1}H NMR (400 mHz, D_2O): δ 4.07 (t, 2H), 4.04 (t, 2H), 3.3 (m, 2H), 3.13 (s, 9H), 2.39 (t, 2H), 2.36 (t, 2H), 1.87 (m, 4H), 1.64 (m, 4H), 1.40−1.26 (m, 18H), 0.86 (t, 3H). ^{13}C NMR (100 mHz, d_6-DMSO): δ 172.44, 172.43, 65.06, 63.77, 63.64, 52.05, 32.52 (2 C's), 31.28, 28.91 (2 C's), 28.68, 28.62, 28.08, 27.83, 25.34, 24.88, 22.08 (2 C's), 21.92, 19.91, 13.93. Mass spec. theory $(M - Br)^+$ 414.3583 amu, found 414.3573 amu. Elemental analysis: theory (surfactant **D** + $1H_2O$) 56.33% C, 9.86% H, 2.74% N; found 56.57% C, 9.74% H, 2.90% N.

Surfactant E (10). Yield = 78.0%, fluffy white powder. ^{1}H NMR (400 mHz, d_6-DMSO): δ 4.029 (t, 2H), 3.999 (t, 2H), 3.253 (m, 2H), 3.028 (s, 9H), 2.262 (dt, 4H), 1.657 (m, 2H), 1.6−1.45 (m, 6H), 1.35−1.2 (m, 12H), 1.168 (t, 3H). ^{13}C NMR (100 mHz, d_6-DMSO): δ 172.90, 172.85, 65.16, 63.61, 59.64, 52.06, 33.40, 28.37 (2 C's), 28.08, 28.03, 25.66, 25.26 (2 C's), 24.28, 24.24, 21.98 (2 C's), 14.12. Mass spec. theory $(M - Br)^+$ 372.3114 amu, found 372.3112 amu. Elemental analysis: theory (2surfactant **E** + $1H_2O$) 54.75% C, 9.42% H, 3.04% N; found 54.92% C, 9.38% H, 3.10% N.

Surfactant F (14), Yield = 92%, fluffy white powder. ^{1}H NMR (400 mHz, d_6-DMSO): δ 4.070 (t, 2H), 3.385 (m, 2H), 3.076 (s, 9H), 2.305 (t, 2H), 2.023 (m, 2H), 1.516 (m, 2H), 1.235 (m, 16H), 0.850 (t, 3H). ^{13}C NMR (100 mHz, d_6-DMSO): δ 172.8, 60.8, 52.2, 33.4, 31.3, 29.0, 28.9, 28.7, 28.5, 24.3, 22.1, 13.9. Mass spec. theory $(M - Br)^+$ 300.2903 amu, found 300.2901 amu. Elemental analysis: theory (3surfactant **F** + $1H_2O$) 56.21% C, 10.29% H, 3.58% N; found 56.41% C, 10.02% H, 3.36% N.

8-Ethoxy-8-Oxooctanoic Acid (6).[26,33] First, 12.8732 g of suberic acid was added to a 1 L round-bottomed flask containing 360 mL of H_2O, 300 mL of ethanol, and 3 mL of concentrated H_2SO_4. The reaction was continuously extracted with cyclohexane for 2 days using a Kimble Kontes continuous liquid/liquid, lighter than water extraction apparatus. After 2 days, the layers were separated and the cyclohexane was allowed to cool. Upon cooling, the cyclohexane was filtered through fine filter paper to remove any excess suberic acid that had precipitated out of solution. After concentrating the cyclohexane layer to 150 mL, 4 × 200 mL of a saturated $NaHCO_3$ solution was used to extract the mono-esterified compound from the cyclohexane layer. The water was collected, and the pH was adjusted to 2 using dilute HCl. Four 100 mL portions of ether were used to extract the product from the aqueous layer. The ether layer was dried over $MgSO_4$, and the solvent was stripped to yield 7.0737 g (47.3%) of a yellow oil. ^{1}H NMR (400 mHz, $CDCl_3$): δ 4.12 (q, 2H), 2.33 (t, 2H), 2.28 (t, 2H), 1.61 (m, 4H), 1.34 (m, 4H), 1.24 (t, 3H). ^{13}C NMR (100 mHz, $CDCl_3$): δ 180.27, 174.03, 60.45, 34.42, 34.15, 28.90, 28.83, 24.90, 24.62, 14.41.

Acknowledgment. This work was supported by the Petroleum Research Foundation and the Army Research Office.

JA040105S

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