A Micelle That Is Insensitive to Its Ionization State. Relevance to the Micelle Wetness Problem

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In matters of micelle structure, neutrality seems impossible. This was driven home forcefully when, in the late 1970s and early 1980s, we proposed that micelles are porous, water-permeated structures[1] (a hypothesis that ran counter to the classical Hartley model[2] depicting micelles as "oil droplets with ionic coats"). Response to the proposal was both strongly supportive[3] and antagonistic,[4] and to this day the issue has not been fully resolved.

Among the evidence favoring a "wet micelle", perhaps the most pursuasive came from NMR studies of the acetylenic surfactants drawn below.[5]

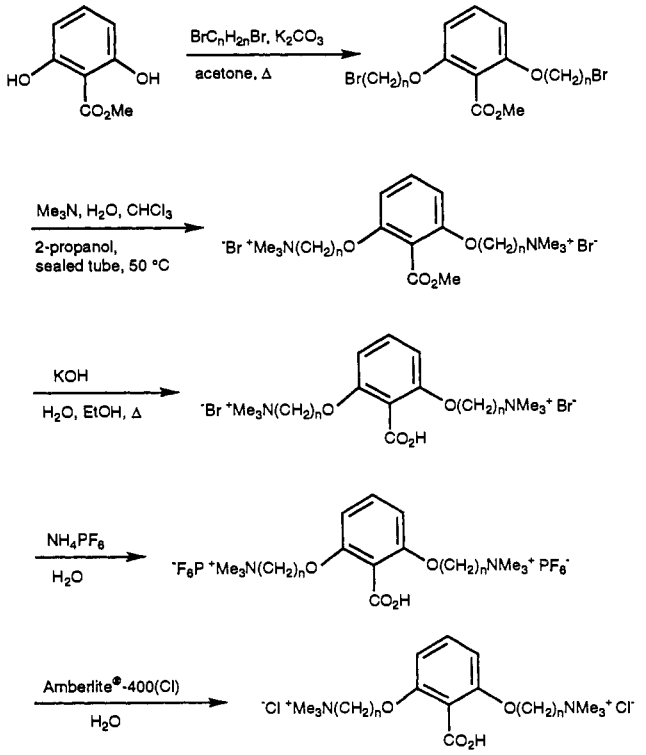
$$HC{\equiv}CCD_2(CH_2)_{10}N^+(CH_3)_3$$

$$HC{\equiv}CCD_2(CH_2)_{10}OSO_3^-$$

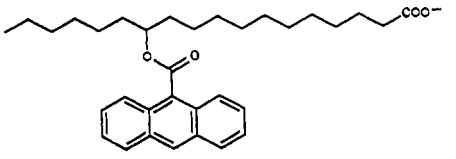
Chemical shifts of the –C≡CH proton of micellized surfactants in D_2O appeared at 2.10–2.16 ppm (typical of protic solvents and far downfield from the 1.6–1.8 ppm expected for a hydrocarbon solvent or for a neat alkyne). There are two opposing explanations for this result: (a) the terminal acetylene protons could be embedded in a wet micelle interior ("interior" being defined as any point inside the Stern layer) or (b) the majority of acetylenic groups might loop out of a dry interior into the external water. We favor the first rationale because the surfactants were found to have normal critical micelle concentrations (cmcs). If "water-seeking" acetylenic groups had induced anomalous looping, then the surfactant chain length would have been effectively halved, and the cmcs should have increased. (As a general rule, the cmc increases 2-fold when a chain is shortened by one carbon).[6] Note that our preference for a wet micelle interior in no way precludes the acetylenes from sampling the interface. The chemical shifts represent, however, a weighted average from all loci, with the interface making, in our view, only a small contribution.

Over the years, many features of the "brush heap" micelle model (*e.g.*, nonradial distribution, surface roughness, etc.) have quietly infused into the literature.[7] Nonetheless, uncertainty with regard to "wetness" persists, as is evident from recent work of Melo et al.[8] These authors used 12-(9-anthroyloxy)stearic acid to probe the water content of cationic and anionic micelles. The idea was to incorporate the compound into micelles and to measure the resulting fluorescence emission and the quenching by water.

Scheme I



In this manner the water content could be evaluated. Dodecyltrimethylammonium chloride was found to have a water content



of 19 M (from λ_f data) or 1–6 M (from quenching data). For sodium dodecyl sulfate (SDS), the water content corresponds to 2.5 M (from λ_f data) or 17–22 M (from quenching data). Supplementary NMR results on SDS indicated a low probability that the probe moiety resides at the interface.[8]

The obvious conclusion from the above data, namely that micelle interiors are wet, was summarily dismissed in favor of other possibilities[8] (including one in which the anthroyloxy group perturbs the local environment and allows the entry of water). Unfortunately, ambiguity in probe work is inescapable. Indeed, our use of a sterically and electronically innocuous acetylene probe reflects an attempt to minimize probe-induced artifacts. In any event, further examination of the wetness problem was clearly in order, and we report here our most recent findings.

Consider a surfactant which, upon micellization, buries a carboxyl substituent in the micelle interior. If the interior is in fact dry and nonpolar, then the carboxyl group should manifest an unusually high pK_a (similar to that of carboxyl groups embedded in hydrophobic regions of proteins).[9] Moreover, the cmcs of the surfactant should be vastly different according to whether the carboxyl is ionized or not. Water within the micelle interior would, or course, mitigate these effects. With this premise, we examined surfactant **I** (n = 8, 12, and 16), whose synthesis is given in Scheme 1.[10]

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(7) For a recent computer simulation of a surfactant micelle showing these features, see: Smit, B.; Esselink, K.; Hilbers, P. A. J.; van Os, N. M.; Rupert, L. A. M.; Szleifer, I. *Langmuir* **1993**, *9*, 9.

(8) Melo, E. C. C.; Costa, S. M. B.; Macanita, A. L.; Santos, H. *J. Colloid Interface Sci.* **1991**, *141*, 439.

(9) Steitz, T. A.; Henderson, R.; Blow, D. M. *J. Mol. Biol.* **1969**, *46*, 337. Tanford, C. *Adv. Protein Chem.* **1962**, *17*, 70 lists a pK_a = 7.3 for two carboxyl side chains of β-lactoglobin. See also: Urry, D. W. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 819.

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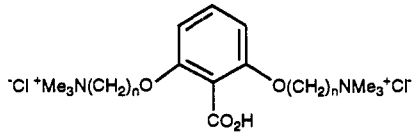

I

Critical micelle concentrations at pH = 1.6 (determined tensiometrically) were found to equal >1.6 × 10^{-2}, 1.1 × 10^{-4}, and 6.8 × 10^{-6} M for I-8, I-12, and I-16, respectively. More interestingly, I-16 has cmcs that differ by less than a factor of 2 over a large pH range: cmc = 6.8 × 10^{-6} M (pH = 1.6); cmc = 6.8 × 10^{-6} M (pH = 4.0); cmc = 8.9 × 10^{-6} M (pH = 7.0); and cmc = 1.1 × 10^{-5} M (pH = 8.8). Surface tensions at the four cmcs were identical (45 ± 2 dyn/cm), while hydrodynamic diameters by quasielastic light scattering were 46 ± 10 Å at both pH = 1.8 and 7.0. It appears, therefore, that aggregation of I-16 is unresponsive to the ionic state of the carboxyl.

The pK_a of 2,6-dibutoxybenzoic acid (measured spectrophotometrically at 280 nm) is 3.73. Spectrophotometric titration of I-8 at 9.5 × 10^{-5} M (where the compound is totally monomeric) gave a pK_a of 3.60. Titration of I-12 at 1.5 × 10^{-4} M (near the cmc where there exists an appreciable percentage of both monomeric and micellar surfactant) gave a pK_a of 3.78. The corresponding titration curves were sigmoidal, and the usual plot of log[A − A^-)/(AH − A)] was linear. Similarly, titration of I-16 at 4.7 × 10^{-5} M (above the cmc) gave rather normal plots (Figure 1) and a pK_a of 3.77. At higher concentrations, 9.2 × 10^{-5} and 3.9 × 10^{-4} M, the titration plots became distorted with no visible inflection point (Figure 2). Although a pK_a cannot be easily extracted from the data, it is clear that the carboxyl groups have their pK_a values shifted upward by no more than a unit even at 57 times the cmc.

In summary, we have constructed a micelle that is surprisingly insensitive to its ionization state. *Ionization has little effect upon the cmc, and micellization has little effect upon the pK_a.* A likely explanation for these facts is that micelles are loose molecular "brush heaps" with the interstices occupied by water. The carboxyl groups reside in the aqueous interstices, and, as a consequence, the ionization and aggregation processes operate independently.

One must now ask two questions: (a) Are there other explanations for the insensitivity of I to its ionization state? (b) Are the data with I germane to "normal" micelles? With regard to the first question, it is possible to imagine, as an alternative, that *both* chains simultaneously distort themselves so as to place all three polar groups (the carboxyl and two cationic nitrogens) onto the surface of normal-sized micelles. If this is true, then chain disorder within micelles is more extreme than even we have previously portrayed.[1] With regard to the generality of our conclusions, we can state that by themselves the properties of I cannot be extended to "normal" surfactants. But when the data are combined with those from many other studies (especially the acetylene[5,11] and anthroyloxy[8] probe work), and when economy of explanation is taken into account, one must accept the presence of water molecules (or water aggregates) within the micelle core as a viable hypothesis that has yet to be disproved.[12]

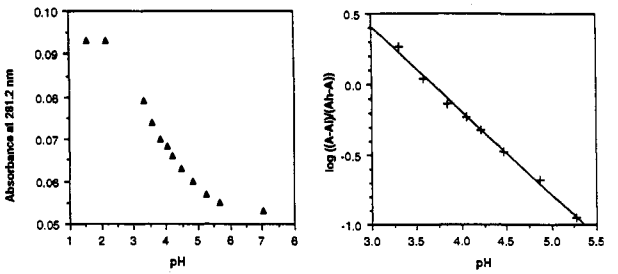

Figure 1. Absorbance *vs* pH plot for 4.7 × 10^{-5} M I-16 (left) and the corresponding linear plot from which a pK_a of 3.77 was obtained (right).

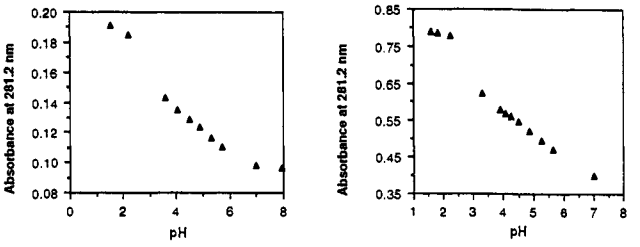

Figure 2. Absorbance *vs* pH plots for 9.2 × 10^{-5} M I-16 (left) and 3.9 × 10^{-4} M I-16 (right).

Acknowledgment. This work was supported by the National Institutes of Health.

(10) Compounds were fully characterized by ^1H and ^{13}C NMR, mass spectrometry, and elemental analyses. For synthetic details, see the 1993 Ph.D. thesis of Corrine E. Mounier (Emory University): Part I. Hindered Rotation about the Amide Bond in Hydrocarbon-Substituted Ureas and Carbamates: Chain Length and Solvent Viscosity Effects. Part II. 2,6-Disubstituted Benzoic Acids and Phenols: Acidity, Complexation, and Aggregation Behavior.

(11) One might argue that the carboxyl of I "drags" water into micellar regions that are normally dry. It is much harder to argue likewise for the acetylenic probe, illustrating the value of using a variety of probe types when constructing a model.

(12) As Howard Gardner has written, "Advances in science can come about only through the positing of detailed models that can be tested, refined, and refuted". Thus far all our attempts to refute the "wet micelle" model have failed.