

ond-order rate constants for pyridine and imidazole promotion of the reactions of the Ni(II) complex of V at 85 °C are 20 000- and 80 000-fold larger than those for reactions of *p*-nitrophenyl phosphate²⁷ at 39 °C. Therefore, the effect of the metal ion is profound.

High concentrations of Mg²⁺ or Ca²⁺ (0.33 M) were recently reported¹⁹ to have only a small catalytic effect on the pyridine-catalyzed hydrolysis of *p*-nitrophenyl phosphate. It was concluded that metal ion binding to the phosphate oxygens has little effect on the ability of pyridine to attack phosphorus as a nucleophile. In contrast, pyridine is a good catalyst in the hydrolysis of the Ni^{II} complex of V where binding of the metal ion is strong, even though no reaction can be observed in the absence of the metal ion.

Alkaline Phosphatase. The mechanisms of metalloenzyme-catalyzed phosphate ester hydrolysis or phosphoryl group transfer are not understood.⁴⁵ However, most of the proposals that have been put forth involve the metal ion in some manner. For example, it was suggested that the zinc ion in the active site of alkaline phosphatase coordinates the two negative charges of a phosphomonoester dianion and thereby enhances nucleophilic attack of a serine hydroxyl group.^{11,46} A phosphorylated serine is an intermediate in the reaction. Others have pointed out that the Zn^{II} may enhance metaphosphate elimination;¹⁰ serine is then phosphorylated by metaphosphate capture. The key question would appear to concern binding of the metal ion to the phosphate ester substrate. If Zn^{II} binds to the leaving-group oxygen, then the mechanism probably involves metaphosphate elimination. If, however, the leaving group is not complexed but the other oxygens are chelated, then the mechanism probably involves a direct nu-

cleophilic attack by the serine hydroxyl on phosphorus. This is, of course, based on the consideration that the metal ion is directly complexed to the phosphomonoester substrate.⁴⁷⁻⁴⁹ If a metal ion bound water molecule is located between the metal ion and the substrate, then the mechanistic considerations will be unchanged, and the water molecule can then act as a general acid to facilitate either nucleophilic attack by serine or metaphosphate elimination.⁵⁰ The present work shows that when the leaving-group oxygen of a phosphomonoester is not significantly chelated in a 1:1 complex, a strongly bound metal ion will nevertheless produce large rate enhancements in the hydrolysis reactions and will lead to catalytic processes involving water and amines that proceed most likely by nucleophilic pathways. The conceptually simplest mechanism in the alkaline phosphatase catalyzed hydrolysis of phosphomonoesters would be that in which the neutral serine hydroxyl attacks at phosphorus.

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Registry No. KCl, 7447-40-7; Ni²⁺, 14701-22-5; Co²⁺, 22541-53-3; Zn²⁺, 23713-49-7; 1,10-phenanthroline methiodide, 112399-14-1; 1-methyl-2-*o*-phenanthrolone, 1-methyl-2-*o*-phenanthrolone; 2-chloro-1,10-phenanthroline, 7089-68-1; 2-phenoxy-1,10-phenanthroline, 22426-17-1; 2-hydroxy-1,10-phenanthroline, 92695-50-6; 2-(1,10-phenanthrolyl)phosphate, 112399-15-2.

(47) Some of the evidence for such direct binding is summarized in ref 11b.

(48) X-ray crystallographic studies have indicated that direct binding of Zn^{II} in the enzyme active site with a phosphomonoester is structurally feasible: Sowadski, J. M.; Handschumacher, M. D.; Murthy, H. M. K.; Foster, B. A.; Wyckoff, H. W. *J. Mol. Biol.* **1985**, *186*, 417.

(49) Otvos, J. D.; Alger, J. R.; Coleman, J. E.; Armitage, I. M. *J. Biol. Chem.* **1979**, *254*, 1778 and references therein.

(50) For a mechanism of that type see: Cleland, W. W. *Adv. Enzymol. Relat. Areas Mol. Biol.* **1977**, *45*, 273.

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Semifluorinated Hydrocarbons: Primitive Surfactant Molecules

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Abstract: F(CF₂)₈(CH₂)₁₂H and F(CF₂)₈(CH₂)₁₆H form reversed micelles in perfluorotributylamine and perfluorooctane, respectively. Static and dynamic light scattering, NMR, and fluorescence and absorbance probe solubilization demonstrate the presence of micelles. There is also preliminary evidence of normal micelle formation by F(CF₂)₈(CH₂)₁₆H and F(CF₂)₁₀(CH₂)₁₆H in toluene. These are the first examples of micelle formation by nonpolar low molecular weight molecules and they demonstrate that semifluorinated hydrocarbons are a new class of surfactant.

Surfactant solutions, particularly those in concentration regimes which result in the formation of association aggregates (micelles, reversed micelles, vesicles, microemulsions), are important in diverse applications. The dispersed pseudophase of complementary "polarity" provided by the aggregates often conveys properties to surfactant solutions that are inaccessible to single or mixed molecular solvent systems. In part, the rational design and selection of surfactants to achieve specified aggregate architectures can be based on simple hard-core geometric-packing arguments.^{1,2} However, as with molecular fluids, even though gross structural

issues largely devolve to hard-core packing considerations, the thermodynamic properties of the aggregates critically depend on the intermolecular energetics of the amphiphilic molecule. Yet, in contrast to the situation encountered with pure molecular fluids, little effort has been expended in the development and study of functionally primitive surfactant systems. By functionally primitive we mean aprotic species which possess no (or minimal) permanent molecular dipole. Without such benchmark examples available for study, molecular theories of surfactant aggregation must incorporate rather severe approximations to treat experimental data. In this regard, concordance between theory and experiment must be viewed with caution.

The detailed structural and energetic requirements for a molecule to display surfactant behavior have yet to be satisfactorily elucidated even though the qualitative guidelines of surfactant

(1) Israelachvili, J. N.; Mitchell, D. J.; Ninham, B. W. *J. Chem. Soc., Faraday Trans. 2* **1976**, *72*, 1525-68.

(2) Mitchell, D. J.; Ninham, B. W. *J. Chem. Soc., Faraday Trans. 2* **1981**, *77*, 601-29.

architecture are well characterized. The basic structural characteristic of a surfactant is a diblock architecture comprised of "immiscible" components.³ However, to use the language of regular solution theory, the disparity in the cohesive energy densities required of the two blocks to yield amphiphilic behavior is not known. In fact, rather basic questions such as the role of solvent hydrogen bond structure in promoting micelle formation in dipolar fluids remain unresolved (see e.g. ref 4). One feature common to virtually all research performed in surfactant solution chemistry is the electrostatic complexity of the molecular interactions within association aggregates. While this mirrors the nature of systems of practical utility, it likely serves to cloud questions of a general conceptual form. Microphase segregation in block copolymer systems⁵⁻¹⁰ to form polymer micelles (as well as higher aggregates) suggests that traditional concepts of surfactant structural requirements are too parochial and conceivably a reflection of the limited range of solvent and surfactant media studied. Micelle formation by styrene-butadiene block copolymer in butadiene homopolymer⁵⁻⁷ demonstrates that nonpolar *high molecular weight* species are capable of micellar self-assembly. Fundamentally, differences in the phase equilibria of multicomponent polymeric and monomeric fluids are manifested in degree rather than kind. Thus, a priori, there is no reason to expect that appropriately designed nonpolar low molecular weight species are incapable of exhibiting amphiphilic character.

As part of a general program on surfactant self-assembly in low cohesive energy density media (nonpolar liquids and supercritical fluids), we have initiated a systematic examination of the key features that relate the thermodynamics of aggregation to functionalization of the surfactant. Solute-solvent interaction energies are necessarily lower in absolute magnitude in low cohesive energy density media than in highly polar fluids. Thus, the energy/entropy balance governing the free energy of self-assembly (versus phase separation) is much more delicate. A critical aspect of this work is the ability to tailor the energetics of self-assembly via the controlled introduction of functional group dipolarity into the surfactant structure. In the first stage of this research we address the question of whether it is possible for a nonpolar low molecular weight solute to undergo micellar assembly.

Recent work by Rabolt and co-workers¹¹⁻¹³ has provided indications that semifluorinated hydrocarbons, $F(CF_2)_m(CH_2)_nH$, behave as prototype surfactant molecules. The key observation made by Rabolt et al. was that equilibration of a semifluorinated hydrocarbon with an *n*-alkane resulted in the formation of what was termed a "gel" phase. An examination of the literature reveals that, in very crude terms, semifluorinated hydrocarbons meet the quintessential structural requirement of an immiscible component diblock structure even though the molecule itself is nonpolar.¹⁴ The significant nonideality of alkane/perfluoroalkane mixtures

has been well documented for many years,^{15,16} while recent research on micelles formed by fluorocarbon/hydrocarbon surfactant mixtures^{17,18} offers compelling evidence of a high degree of segregation of the two surfactants. In addition to the gel phase formed from binary semifluorinated hydrocarbon/alkane mixtures noted above, Mahler et al.¹⁹ have observed and characterized a smectic liquid crystalline phase formed by (perfluorodecyl)decane. On the basis of these observations, Mahler and co-workers characterized semifluorinated hydrocarbons as amphiphilic. However, while such behavior is typical of conventional amphiphilic systems, many liquid crystalline materials do not display any of the characteristics associated with surfactants. In the present work we provide direct evidence of the amphiphilicity of semifluorinated hydrocarbons dissolved in perfluorinated liquids.

Experimental Section

Semifluorinated hydrocarbons (we designate $F(CF_2)_m(CH_2)_nH$ hereafter as F_mH_n) of varying chain-length ratios have been prepared with the methods outlined by Rabolt et al.^{11,12} The synthetic strategy involves an azobis(isobutyronitrile) initiated free-radical addition of 1-perfluoroalkyl iodide to 1-alkene followed by reductive dehydrohalogenation. Perfluoroalkyl iodides (alkyl = octyl, decyl), perfluorohexane, and perfluorotributylamine were obtained from PCR Inc. (Gainesville, FL). 1-Alkenes were obtained from Aldrich Chemical Co. (Milwaukee, WI) or Alfa Products (Danvers, MA). Product identity was confirmed by ¹H and ¹⁹F NMR (Bruker/IBM AF300, 300 MHz) and mass spectrometry (VG Instruments 70-G). Product purity was verified by supercritical-fluid chromatography (CO₂ mobile phase). Toluene, perfluorohexane, and perfluorotributylamine were examined as solvent media. Solvents were distilled and filtered (0.45- μ m nylon membrane, Rainin Inc., Woburn, MA) prior to use.

Light-scattering experiments were performed on a modified Wyatt Technology Dawn F (Wyatt Technology Inc., Santa Barbara, CA) light-scattering photometer using a stabilized HeCd laser source (441.6 nm, Liconix Model 4210N, 0.3-mm beam diameter, Liconix Model 50SA power stabilizer; Liconix Inc., Sunnyvale, CA). This photometer is a fixed multiangle fiber optic coupled instrument. Scattering angles of 27.5 and 96.7° were used for both the static and dynamic light scattering measurements performed on this instrument. Static light scattering measurements were also performed on an SLM-8000C (SLM Instruments Inc., Urbana, IL) fluorometer with right-angle geometry. Dynamic light scattering measurements employed a Langley-Ford 1096 autocorrelator (Langley-Ford Instruments, Amherst, MA) interfaced to an IBM-PC for off-line cumulant analysis.²⁰ Samples for light scattering were filtered (0.2- μ m Gelman ACRO LC13, Gelman Sciences, Ann Arbor, MI) directly into the sample container (28-mm scintillation vials (Fisher) or 1.00-cm quartz cuvettes) and examined under ambient conditions (23 \pm 1 °C).

¹H NMR chemical shift measurements were performed on samples identical with those examined by light scattering. The NMR chemical shift measurements were performed at 30 \pm 0.1 °C.

Fluorescence probe solubilization studies were performed on the SLM-8000C fluorometer equipped with a temperature-controlled cell block. Samples were purged with solvent-saturated N₂ prior to examination. Solute probes examined included pyrene (Aldrich Chemical Co.), 9-methylanthracene (Molecular Probes Inc.), coronene (Aldrich Chemical Co.), rhodamine B (Chem Service), ruthenium(III) tris(bipyridyl) chloride (ICN Biomedical Inc., K & K Labs), and 25-(NBD-methylamino)-27-norcholesterol oleate (NBD = 7-nitrobenz-2-oxa-1,3-diazol-4-yl), and 3-hexadecanoyl-7-(dimethylamino)coumarin (Molecular Probes Inc.).

UV-visible absorbance measurements were performed on a Beckman DU-7 spectrophotometer (Beckman Instruments, Fullerton, CA) equipped with a thermostated cell compartment.

While we have performed preliminary studies on a number of F_mH_n systems, the most detailed work accomplished to date has involved F_8H_{12} .

Results

Fluorescence probe solubilization provides the clearest evidence of micelle formation in the F_8H_{12} /perfluorotributylamine system.

(3) We are implicitly ignoring higher block architectures, e.g. triblock, which, in fact, do display typical surfactant characteristics.

(4) Beesley, A. H.; Evans, D. F.; Lauglin, R. G. *J. Phys. Chem.* **1988**, *92*, 791-3.

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(14) The claim that semifluorinated hydrocarbons are strictly nonpolar is based on operational results rather than a determination of dielectric properties. Solvatochromic experiments indicate a polarity very similar to *n*-alkanes (as quantified by the π^* scale). Parenthetically, we should note that the π^* scale is rather sensitive to the presence of dipolar functionality. Further, chromatographic studies of semifluorinated hydrocarbon retention (supercritical CO₂ mobile phase, octadecylsilane bonded stationary phase) reveal the free energy of transfer of semifluorinated hydrocarbons is intermediate to that of perfluoro- and perhydrocarbons of the same total chain length. Thus, intuitive expectation is achieved.

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(20) Koppel, D. E. *J. Chem. Phys.* **1972**, *57*, 4814-20.

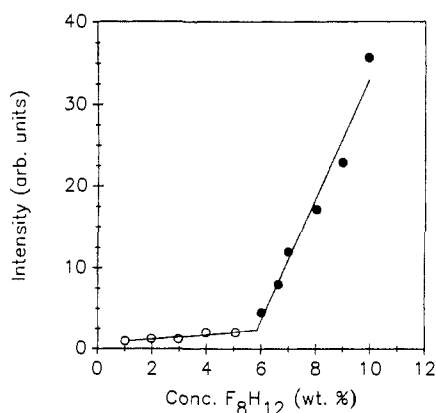


Figure 1. Plot of fluorescence intensity 25-(NBD-methylamino)-27-norcholesteryl oleate against weight percent concentration of $F(CF_2)_8(CH_2)_{12}H$ in perfluorotributylamine. Excitation was at 475 nm and emission intensity was monitored at 510 nm.

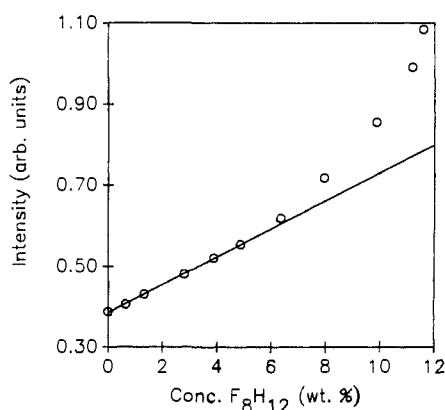


Figure 2. Plot of scattered intensity (arbitrary units) against weight percent concentration of $F(CF_2)_8(CH_2)_{12}H$ in perfluorotributylamine. A scattering angle of 96.7° was used.

A major difficulty in performing these experiments was identification of a suitable probe molecule. Polycyclic aromatic probes that are typically employed in polar solvent micellar solutions (pyrene, 9-methylanthracene, coronene) are sufficiently soluble in perfluorotributylamine that the differential solubility enhancement in the presence of a small volume of alkane-like micellar pseudophase is not readily discerned. At the opposite extreme, polar probes employed in studies of dipolar domains in reversed micelles and microemulsions (rhodamine B, Ru^{III} -(bipy) $_3Cl$) are insoluble in both the supporting solvent and alkane core of the reversed micelles formed by F_8H_{12} .²¹ A steroid-based probe (25-(NBD-methylamino)-27-norcholesteryl oleate) proved to possess suitable solubility characteristics for use. A plot of probe fluorescence intensity against F_8H_{12} concentration is shown in Figure 1. The qualitative form of this plot is typical of that encountered with micellar solutions. The formation of a solubilizing micellar pseudophase is signaled by a rapid increase in fluorescence intensity with increasing F_8H_{12} concentration. A critical micelle concentration (CMC) of 5.8 wt % F_8H_{12} in perfluorotributylamine is deduced from the plot in Figure 1. The sharp break in the curve is suggestive of classical micellization (n monomer \leftrightarrow n -mer) as opposed to gradual stepwise aggregation. We anticipate the aggregate formed is a prototype reversed micelle

(21) In referring to micelles formed by F_8H_{12} compounds as either normal or reversed micelles, we have employed a generalization of conventional terminology. Typically, one views the amphiphile as composed of dipolar and nonpolar blocks. This can be generalized to a consideration of the intrinsic relative cohesive energy density (cf Hildebrand solubility parameter approach) of the component blocks with micelle core formation by the low cohesive energy density block yielding normal micelles. The converse leads to reversed micelles. For semifluorinated hydrocarbons, the formation of a micelle with an alkane core involves clustering of the high cohesive energy density block of the molecule, hence the designation as reversed micelles.

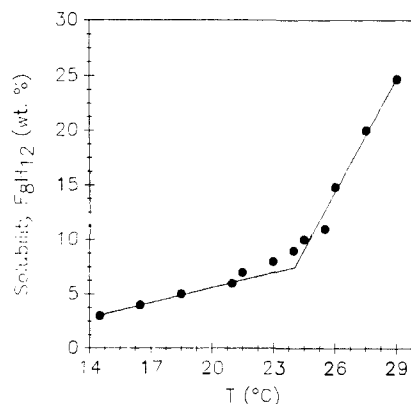


Figure 3. Plot of $F(CF_2)_8(CH_2)_{12}H$ solubility (wt %) in perfluorotributylamine against temperature.

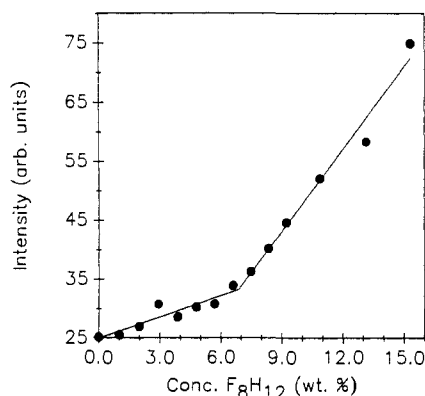


Figure 4. Plot of scattered intensity (arbitrary units) against weight percent concentrations of $F(CF_2)_8(CH_2)_{12}H$ in perfluorotributylamine. A scattering angle of 90° was used and the sample was thermostated at $30^\circ C$.

in which the alkane "head groups" cluster to form a hydrocarbon-like core while the perfluoroalkyl tails reside at the aggregate periphery.

Static light scattering experiments performed on F_8H_{12} /perfluorotributylamine solutions (ambient temperature) reinforce the results obtained by fluorescence. A plot of the scattered light intensity against F_8H_{12} concentration shows a distinct break at approximately 6.0 wt % F_8H_{12} with significant positive deviations from the dilute-solution behavior above this concentration (Figure 2). From 6.0 to approximately 12 wt % F_8H_{12} both static and dynamic light scattering indicate the presence of some type of association aggregate. The ratio of the slope of the scattering curve before and after the CMC can be used to provide a very rough approximation of the *relative* weight of the aggregate,²² i.e. the micelle aggregation number. In contrast to the fluorescence solubilization experiment, these results point to a stepwise association of solution monomer in the formation of the aggregate with aggregation numbers ranging up to 20 just prior to phase separation.

The sharp increase in aggregation number suggested by Figure 2 implies the occurrence of macroscopic aggregates above 11.6 wt % F_8H_{12} . In fact, phase separation is observed in the F_8H_{12} /perfluorotributylamine system at approximately 12 wt % F_8H_{12} under ambient conditions. The concentration range over which the association aggregates are stable is quite narrow (within a factor of 2 of the CMC) under the conditions of the experiment. A determination of F_8H_{12} solubility in perfluorotributylamine as a function of temperature (Figure 3) provides insight to the origin of this behavior. As in conventional micellar systems, a sharp

(22) The use of a simple slope ratio assumes the second virial coefficient (which accounts for intermicellar interactions) is zero and that the specific refractive index increment of the micelles at constant chemical potential (of surfactant monomer and solvent) and constant surfactant concentration are equal.

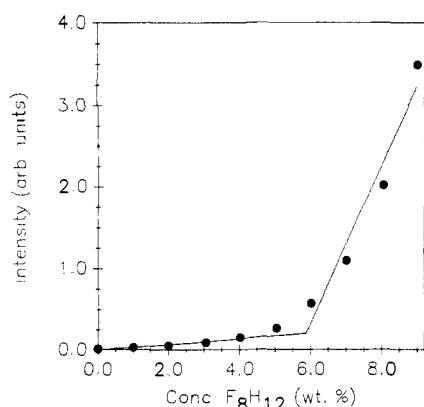


Figure 5. Plot of fluorescence intensity 25-(NBD-methylamino)-27-norcholesterol oleate against weight percent F_8H_{12} concentration in perfluorotributylamine. Excitation was at 475 nm, emission intensity was monitored at 510 nm and the sample was thermostated at 30 °C.

break in the solubility curve occurs at the intersection of the monomer solubility and (temperature dependent) critical micelle concentration curves (Krafft point, see ref 23). Further, the break occurs at an F_8H_{12} concentration of 7.5 wt %, in reasonable agreement with the CMC determined by fluorescence probe solubilization and light scattering. However, as is apparent from Figure 3, the initial fluorescence probe solubilization and light scattering experiments were performed in proximity to the Krafft temperature (24.0 °C). Static light scattering measurements were repeated at 30 °C with only a minor shift in the CMC (Figure 4) to 6.9 wt %. In contrast to the results presented in Figure 2, the intensity is linear well beyond the CMC with eventual phase separation achieved at *much* higher concentration (ca. 25 wt %). Figures 2 and 4 both suggest the aggregates formed are rather small with aggregation numbers in the range of 4–6. Fluorescence probe solubilization experiments performed at 30 °C (Figure 5) yield results virtually equivalent to those obtained at ambient temperature with a CMC of 5.9 wt %. We emphasize that the results shown in Figures 1–5 are equilibrium results and are not due to supersaturated solutions or kinetically metastable aggregates; thermal cycling between solution and phase-separated systems does not alter the ambient or higher temperature results.

Attempts to characterize the aggregate size by dynamic light scattering were unsuccessful because reactive diffusion²⁴ dominates micelle transport in this system. Dynamic light scattering measures center of mass transport of the scattering particles. For particles which exist as *dynamic entities*, such as micelles, the center of mass transport may proceed either by an intact particle translational motion *or* via exchange of surfactant monomer between the solution and the particle. The latter pathway is anticipated to be significant in micellar solutions with a high CMC and low aggregation number.²⁵ According to the static light scattering data, this condition is achieved for F_8H_{12} /perfluorotributylamine. If the particle transport is completely dominated by micelle/solution monomer exchange, the apparent hydrodynamic radius should approach that of the solution monomer.²⁶ The apparent (equivalent sphere) hydrodynamic radius calculated from dynamic light scattering (2.7 Å (stick boundary condition), 4.1 Å (slip boundary condition), F_8H_{12} concentration 7.5 wt % scattering angle 96.7°) is close to that estimated for the F_8H_{12} monomer on the basis of a simple additivity of the component block molar volumes (4.6 Å).²⁷

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(25) The key variable is the *fraction* of surfactant present as monomer. Thus, regardless of CMC and aggregation number, dynamic light scattering experiments in micellar solution will be influenced by reactive diffusion if the experiment is performed in proximity to the CMC.

(26) An implicit assumption here is that diffusional transport of monomer, not micelle/monomer exchange kinetics is the rate-limiting step.

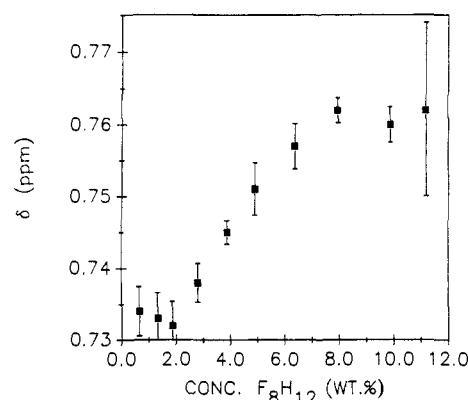


Figure 6. Plot of CH_3 1H chemical shift against weight percent concentration of F_8H_{12} in perfluorotributylamine.

While the dynamic light scattering results are easily rationalized by invoking the mechanism of reactive diffusion, the onset of phase separation at compositions in reasonable proximity to the CMC prevents a detailed study of the composition dependence of the apparent hydrodynamic radius to support this contention. We have sought to address this issue indirectly by monitoring the effect of solubilizing a significant volume of a normally insoluble compound on the observed hydrodynamic radius. Decane is virtually insoluble in pure perfluorotributylamine. The addition of 0.22 wt % decane to a 7.5 wt % F_8H_{12} /perfluorotributylamine solution increases the apparent hydrodynamic radius of the aggregate to 4.2 Å (6.3 Å slip boundary condition). This is a 50% increase over that observed at the same F_8H_{12} concentration in the absence of decane. Whether this growth is real or simply a reflection that decane is unable to contribute to reactive diffusion is uncertain. In either case, the observed increase in hydrodynamic radius with decane solubilization supports the view of reactive diffusion dominating transport in pure F_8H_{12} /perfluorotributylamine solutions and that the dynamic light scattering results are not spurious.

Further addition of decane to a level of 0.49 wt % leads to pronounced Tyndall scattering. Dynamic light scattering indicates the presence of (decane) droplets with a radius of the order of 2750 Å. Over the course of weeks, aging of the sample is apparent. The temporal evolution of the mean apparent hydrodynamic radius suggests slow droplet coalescence. Polydispersity in the size distribution (signaled by an increase in the magnitude of the quadratic term of a second order cumulants analysis) increases over time and stabilizes after 2 weeks. It is not clear whether this aging phenomenon is entirely a result of excessive loading of the F_8H_{12} /perfluorotributylamine solution with decane or if the droplets are inherently (thermodynamically) unstable. A biexponential analysis of the light-scattering autocorrelation function shows that a significant population of droplets with a radius of 2900 Å persists after a number of weeks. The fact that the stable (?) micro-/macroscopic droplets form in the presence of large amounts of decane provides further *indirect* evidence of the amphiphilic character of F_8H_{12} . This conclusion is additionally supported by a qualitative inspection of the wetting characteristics of an F_8H_{12} /perfluorotributylamine solution compared with pure perfluorotributylamine equilibrated with excess decane. The interfacial tension between the two phases is significantly reduced with F_8H_{12} in solution.

NMR chemical shift measurements provide an ambiguous indication of aggregate formation. Figure 6 shows a plot of the terminal methyl 1H chemical shift against F_8H_{12} concentration.

(27) The use of slip versus stick boundary conditions in this instance is problematic. Clearly, in weakly interactive media such as perfluorinated liquids, achievement of slip conditions is reasonable. However, we are clearly in a regime beyond the strict applicability of hydrodynamic treatments; we are examining molecular diffusion. It seems most appropriate to view these results as order of magnitude measures. In this context, the absolute values obtained are less important than are the changes noted with, for example, decane solubilization.

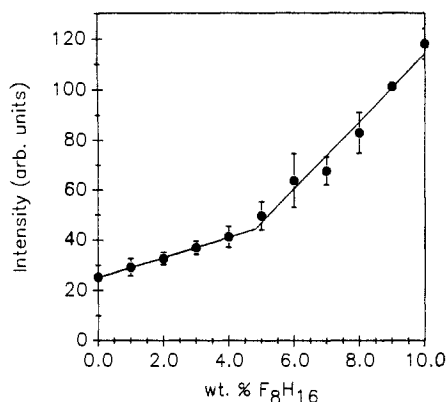


Figure 7. Plot of scattered intensity (arbitrary units) against weight percent concentration of $F(CF_2)_8(CH_2)_{16}H$ in perfluorooctane. A scattering angle of 90° was used. The sample was thermostated at $40^\circ C$.

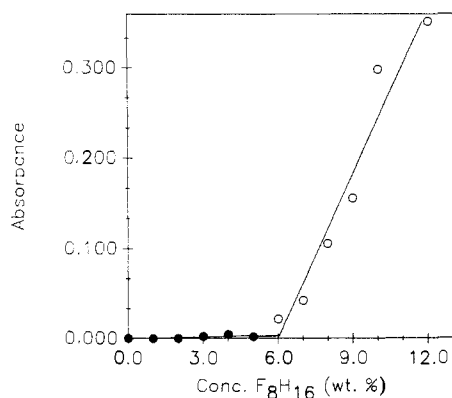


Figure 8. Plot of absorbance due to 3-hexadecanoyl-7-(dimethylamino)coumarin against weight percent concentration of $F(CF_2)_8(C-H_2)_{16}H$ in perfluorooctane. Absorbance was monitored at 407 nm and the sample was thermostated at $40^\circ C$.

The general trend established in Figure 6 is consistent with the F_8H_{12} methyl group residing in an increasingly alkane-like environment as the F_8H_{12} concentration increases. Note however that at F_8H_{12} concentrations above the CMC deduced from fluorescence and light scattering, the chemical shift becomes independent of concentration. The meaning of this particular result is unclear. Generally, the observed chemical shift is anticipated to be a mass weighted average of micellar and solution monomer chemical shifts. Although the concentration dependence of the 1H methyl chemical shift should be different above and below the CMC, one would *not* expect the chemical shift to be independent of concentration above the CMC.

The results described above are not limited to the F_8H_{12} /perfluorotributylamine system. Similar results are obtained from systems such as F_8H_{16} /perfluorooctane. Figure 7 presents static light scattering results obtained from F_8H_{16} /perfluorooctane solutions at $40^\circ C$ with a critical micelle concentration of roughly 4.5 wt %. Phase separation occurs between 20 and 25 wt % at this temperature. The light-scattering results are again quantitatively confirmed by (absorbance) probe solubilization (Figure 8) with 3-hexadecanoyl-7-(dimethylamino)coumarin as the probe (CMC estimated as 6.1 wt %).

The unambiguous result from the combined techniques of absorbance and fluorescence probe solubilization, light scattering, and NMR is that semifluorinated hydrocarbon/fluorocarbon mixtures do not form binary molecular solutions at high solute concentration. The benchmark characteristic of a micellar solution, to behave as a solubilizing dispersed pseudophase, is indeed observed in these systems. The estimated aggregation numbers of the micelles are on the order of 4–6. While these numbers are small, they are of the same order as observed for some conventional micellar systems (e.g. bile salt micelles). A detailed analysis of the aggregate characteristics by fluorescence probe-*quench* and probe-solubilization techniques and osmometry is in progress.

Analogous results are observed via light scattering (static as well as dynamic) with toluene as the solvent and F_8H_{16} or $F_{10}H_{16}$ as the solute. In this case a normal micelle comprised of a perfluoroalkyl tail and alkane periphery is expected. However, confirmation of these observations by independent methods awaits. We should also point out that in contrast to the behavior observed in perfluorotributylamine, F_8H_{12} does appear to form a molecular solution with perfluorohexane as the solvent in the concentration range (<10 wt %) examined thus far. The lack of surfactant activity in perfluorohexane is consistent with critical solution temperatures for perfluorotributylamine/alkane mixtures being higher than for perfluorohexane/alkane mixtures.²⁸

To summarize, we have observed the first example of micelle formation by a completely nonpolar low molecular weight molecule in a condensed phase. The studies of polymer micelle formation from nonpolar block copolymers and the present work underscore the need to generalize our concepts of the requirements for a molecule to display amphiphilic behavior. The assembly process described above is fundamentally distinct from clustering of nonpolar molecules in nonpolar media in (thermal) proximity to a plait point which has been observed elsewhere.^{29,30} The aggregates are small and stable over a rather narrow concentration range, beyond which phase separation is achieved. In many respects this underscores the view that phenomena such as micellization are, in fact, inhibited phase-separation events. The utility of this type of simple architecture for testing mean field theories of aggregation is clear. In some respects the surfactant molecules studied here possess a distinct advantage over analogous polymeric systems: rational kinetics of assembly and phase separation should be more rapid, the molecular weight of the solution monomer species is well defined, and one is afforded more control in the rational synthetic introduction of functional-group complexity.

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Note Added in Proof: A report of micelle formation by semifluorinated hydrocarbons in alkane media has recently appeared (Pugh, C.; Höpken, J.; Möller, M. *Polym. Prepr. (Am. Chem. Soc., Div. Polym. Chem.)* **1988**, 29(1), 460–1), reinforcing the conclusions presented above.

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