Segmental Motion of Amphipathic Molecules in Aqueous Solutions and Micelles. Application of Natural-Abundance Carbon-13 Partially Relaxed Fourier Transform Nuclear Magnetic Resonance Spectroscopy[1]

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Abstract: Molecular motions in unaggregated and micellar aqueous solutions of several *n*-alkyltrimethylammonium bromides were studied by means of ^{13}C spin–lattice relaxation times (T_1) of individual carbon resonances. The T_1 values were extracted from proton-decoupled natural-abundance ^{13}C partially relaxed Fourier transform nmr spectra. Spin–lattice relaxation times for monomolecular solutions of *n*-hexyl- and *n*-octyltrimethylammonium bromides reveal a slight trend toward increasing segmental mobility as one moves along the chain away from the polar head. Spin–lattice relaxation times for micellar solutions of surfactants exhibit more severe immobilization at the polar end of the molecule. Rod-shaped micelles formed from *n*-hexadecyltrimethylammonium bromide show the same general pattern as observed for spherical micelles, except that modest additional restrictions on segmental mobility are observed.

Amphipathic molecules, those possessing clearly defined regions of both hydrophobic and hydrophilic character,[3] are well known to form a variety of structures in an aqueous environment in which the hydrophilic moiety is exposed to the solvent and the hydrophobic one is hidden from it.[4,5] These include monolayers, micelles, and a variety of smectic mesophases including bilayers. Many such structures derived from simple amphipathic molecules serve as both structural and functional models for more complex ones, including proteins and biomembranes, constructed from the correspondingly more complex biological amphipaths, particularly phospholipids and cholesterol.[6,7]

It has already been clearly demonstrated that the use of ^{13}C spin–lattice relaxation times (T_1) of individual carbons, measured by means of ^{13}C partially relaxed Fourier transform (PRFT) nmr spectra, can be used to determine segmental motions in simple molecules containing linear carbon chains,[8] and in biopolymers,[9–11] model membrane systems,[12] and perhaps some biological membranes.[13] In an effort to exploit the PRFT technique[14] in the case of micelles formed from simple surfactants, we have examined the behavior of three *n*-alkyltrimethylammonium ions. These molecules are attractive since they may be studied as monomeric solutions in water as well as in the form of micelles.

Proton relaxation measurements on micellar systems[15,16] have already been used to separate the contributions from rotational and translational motions to the relaxation process. In ^{13}C T_1 measurements on *protonated* carbons, only the rotational contribution is significant.[17] Moreover, proton relaxation measurements of micelles yielded an "average" proton T_1 of many CH_2 groups,[16] because the various methylene proton resonances were not resolved. In contrast, we report below ^{13}C T_1 values of numerous *resolved* individual carbon resonances. These measurements yield information about differences in rotational mobility along the hydrocarbon chain of a micellar system.

Materials and Methods

n-Alkyltrimethylammonium bromides were prepared from trimethylamine and the corresponding redistilled alkyl bromides as previously described.[18] These surfactants were repeatedly recrystallized from ethanol prior to use. The apparatus and methodology employed to record and analyze the ^{13}C nmr spectra reported below have been previously described.[9,10,17,19] T_1 values were determined from proton-decoupled natural-abundance ^{13}C PRFT spectra.[14]

Results and Discussion

In Figure 1 are recorded the completely proton-decoupled ^{13}C nmr spectra of aqueous solutions of *n*-hexyl-, *n*-octyl-, and *n*-hexadecyltrimethylammonium bromides recorded at 43°. In the case of the *n*-hexyl compound, each carbon atom appears as a resolved resonance. For those surfactants having longer *n*-

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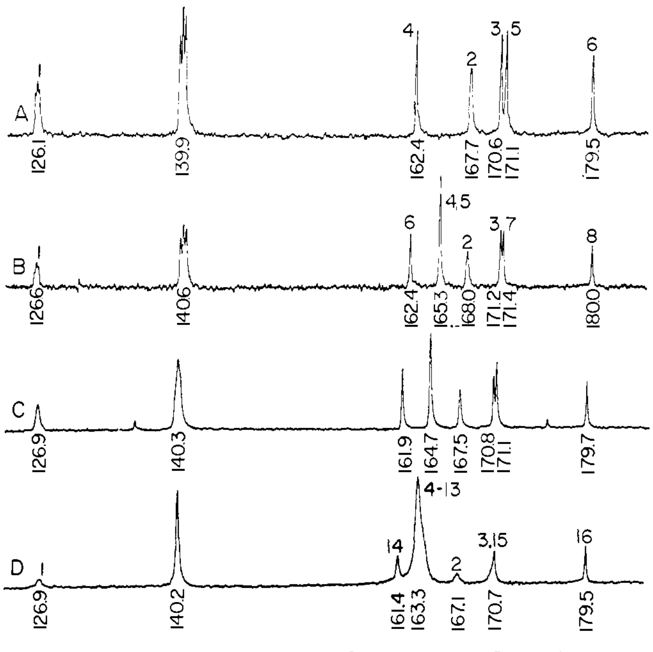

Figure 1. Proton-decoupled natural-abundance ^{13}C Fourier transform nmr spectra of aqueous *n*-alkyltrimethylammonium bromides at 43°, recorded at 15.18 MHz in spinning 20-mm sample tubes, using a 62.5 ppm spectral window and 4096 points in the time-domain. Numbers below the resonances are chemical shifts upfield from CS_2, accurate to ±0.1 ppm, measured on separate samples with dioxane (126.3 ppm) as an internal standard for the *n*-hexyl compound and methanol (144.3 ppm) for the others. Assignments are indicated near the top of each peak. The numbering system for the alkyl chain starts at the $N-CH_2$ carbon. C-1, C-2, and the trimethylammonium resonance (at about 140 ppm) are split or broadened by $^{13}C-^{14}N$ coupling: (A) 1 *M* *n*-hexyltrimethylammonium bromide, after 64 accumulations with a recycle time of 20 sec; (B) 0.2 *M* *n*-octyltrimethylammonium bromide, after 256 accumulations, with a recycle time of 12 sec; (C) 2 *M* *n*-octyltrimethylammonium bromide, after 32 accumulations, with a recycle time of 10 sec; (D) 0.4 *M* *n*-hexadecyltrimethylammonium bromide, after 256 accumulations, with a recycle time of 10 sec.

alkyl chains, the differences in chemical shift of the methylene groups near the center of the chain are insufficient to permit complete resolution of the spectrum. The spectra were readily assigned on the basis of chemical shift data for structurally related compounds,[20,21] splitting of the resonances for those carbon atoms adjacent to the cationic nitrogen reflecting $^{13}C-^{14}N$ scalar coupling, and relative signal intensities. The assignments made on this basis are fully consistent with observed spin–lattice relaxation times, detailed below. Assignments and chemical shift data are given in Figure 1.

Spin–lattice relaxation times (T_1) of the resolved resonances are given in Table I. A qualitative interpretation of the data is analogous to that previously used for liquid 1-decanol.[8] The ^{13}C spin–lattice relaxation of a protonated carbon in a large molecule is overwhelmingly dominated by $^{13}C-^{1}H$ dipole–dipole interactions, and T_1 is given by

$$1/NT_1 = \hbar^2\gamma_C^2\gamma_H^2 r_{CH}^{-6}\tau_{eff} \qquad (1)$$

where N is the number of directly attached hydrogens, γ_C and γ_H are the gyromagnetic ratios of ^{13}C and ^{1}H, respectively, r_{CH} is the C–H bond length, and τ_{eff} is an effective correlation time for rotational reorientation *of the pertinent C–H vector*. Only for a rigid molecule undergoing isotropic rotation is τ_{eff} actually the correlation time for molecular rotation. If the molecular rotation is anisotropic, and/or if internal rotations can occur, τ_{eff} represents an "average" correlation time. NT_1 is inversely proportional to τ_{eff} and thus gives an indication of rotational mobility. As was previously described in the case of liquid 1-decanol,[8] a progressive increase in NT_1 from one end of a flexible molecular chain to the other is an indication of restrictions on the motion at the end of the chain with the small value of NT_1. In liquid 1-decanol, this restriction is caused by intermolecular hydrogen bonding.

Note that the hexyl compound and the dilute solution of the octyl compound contain nonaggregated molecules, while the concentrated solution of the octyl compound consists of spherical micelles. The hexadecyl compound probably forms large rod-shaped micelles which are, however, not organized into a two-dimensional lattice.[5,22]

For *n*-alkyltrimethylammonium bromides present in aqueous solution below their critical micelle concentrations, the trend in spin–lattice relaxation times reveals a slight increase in segmental motion as one moves away from the polar terminus (Table I). This must reflect differential effects of solvation of the polar and nonpolar portions of these amphipaths. A similar trend in T_1 values has been observed for liquid 1-decanol;[8] in this case, however, restriction of mobility at the head group almost certainly arises from intermolecular hydrogen bonding.

Significant changes in spin–lattice relaxation times for *n*-alkyltrimethylammonium bromides accompany micellation of these surfactants (Table I). First, values of NT_1 decrease for all carbon atoms, indicating restrictions on the mobility of the entire chain. This result is certainly expected since the structure of the micelles themselves is inconsistent with isotropic tumbling of individual surfactant molecules. Second, micellation affects values of T_1 for different carbon atoms differentially. This is most evident in the fact that, in the micelle, the site of maximal restriction of mobility is at the polar end of the molecule. Finally, the transition from small spherical micelles to large rod-shaped ones involves modest further decreases in the mobility of the surfactant molecules. This comparison is compromised to the extent that the same surfactant is not involved in the formation of the two types of micelles, but does suggest that measurement of T_1 values may reveal phase transitions in ordered lipid systems.

Values of T_1 measured in this study establish that those carbon atoms occupying the interior of micelles formed from ionic surfactants possess substantial segmental mobility. That is, the micellar interior has properties that approach those of a liquid hydrocarbon. This conclusion is in accord with those based on several different lines of experimental study. First, the thermodynamics of micelle formation suggest a liquid-like interior.[23–25] Specifically, the free energy change per

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Table I. ^{13}C Spin–Lattice Relaxation Times of $[RN(CH_3)_3]^+Br^-$ in Aqueous Solution at 34°

R	Concn, *M*	Type of solution	NT_1, sec[a]							
			CH_3—	—CH_2—	—CH_2—	—$(CH_2)_k$—	—CH_2—	—CH_2—	—CH_2—	—$N(CH_3)_3$
n-Hexyl (*k* = 0)	1.0	Molecular	14.3	8.6	6.3		5.2	5.0	4.4	6.0
n-Octyl (*k* = 2)	0.2	Molecular[b]	12.9		7.8	4.7[c]		4.7	4.7	6.3
n-Octyl (*k* = 2)	2.0[d]	Spherical micelles	10.3	2.9	2.4	1.6[c]	1.0	1.0	0.90	2.6
n-Hexadecyl[e] (*k* = 10)	0.4[f]	Rod-shaped micelles	8.4		1.2			0.68	0.54	1.8

[a] *N* is the number of directly attached hydrogens. T_1 values are accurate to ±10%. Unless otherwise indicated, all NT_1 values are those of totally resolved carbon resonances. [b] Predominantly molecular. Several values of the critical micelle concentration in the range 0.1–0.3 *M* have been reported: P. Mukerjee and K. J. Mysels, *Nat. Stand. Ref. Data Ser., Nat. Bur. Stand.*, No. **36,** 103 (1971). [c] Two-carbon resonance. [d] Critical micelle concentration is about 0.1–0.3 *M* (see footnote *b*). [e] At 41°. [f] Critical micelle concentration is about 10^{-3} *M* (see reference in footnote *b*).

methylene group upon micellation is comparable to that for transfer of a methylene group of an alkane from water to the pure hydrocarbon.[26] Second, the rotational correlation times for stable free radicals dissolved in micelles are only slightly longer than those for the same species in aqueous solution.[26–29] Third, tumbling rates for dyes dissolved in micelles as measured by depolarization of fluorescence are sufficiently rapid to accord with a liquid-like interior for the micelle.[30,31] Finally, differential ultraviolet spectroscopy of micelles formed from chromophoric surfactants suggests a fluid environment for the chromophoric group.[32]

It should be noted that our ^{13}C T_1 values are weighted averages of the T_1 values of unassociated and micellar species.

$$1/T_1 = x_f/T_{1f} + x_m/T_{1m} \tag{2}$$

Here T_1 is the measured ^{13}C T_1 value, T_{1f} and T_{1m} are the relaxation times of free and micellar molecules, respectively, and x_f and x_m are the corresponding mole fractions. Equation 2 is valid when exchange between the free and micellar environment is rapid with respect to $1/T_1$, a condition satisfied here.[33] As a result of the fact that rotational motion of free molecules is faster than that of those in a micellar environment

$$1/T_{1f} < 1/T_{1m} \tag{3}$$

Introduction of eq 3 into (2) yields

$$T_1 > T_{1m} \tag{4}$$

Thus, our observed T_1 values are upper limits to T_{1m}. Consequently, the actual shortening of T_1 at the polar end of the molecule when going from unassociated to micellar species is even greater than our numbers indicate. However, the difference between T_1 and T_{1m} is not expected to be great for the micellar systems we have studied, because x_f is approximately equal to the critical micelle concentration, and thus is much smaller than x_m[34] (Table I).

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Photochemical Rearrangements of α-Methylene Ketones

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Abstract: Preparation and irradiation of 18 α-methylene ketones are described. The resulting products, which are summarized in Table I, are isomeric cyclobutyl ketones, cyclopropyl ketones, and 2-methylenecyclobutanols, formation of which may be explained by eq 1 and 2. In many cases the reaction leads from readily prepared substrates to useful yields of cyclobutyl ketones, including simple, bicyclic, and spirocyclic systems.

In this report we describe the preparation of a variety of open chain α-methylene ketones and identification of the products formed on their irradiation. The results, summarized in Table I and discussed in detail below,[1] can be accounted for by eq 1 and 2. The former involves generation of the familiar type II biradical[2] through carbonyl abstraction of γ hydrogen and sub-

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