JOURNAL OF CHEMICAL & ENGINEERING DATA

ARTICLE

pubs.acs.org/jced

Mesoscale Inhomogeneities in Aqueous Solutions of 3-Methylpyridine and Tertiary Butyl Alcohol

Deepa Subramanian,[†] Dmitry A. Ivanov,[†,⊥] Igor K. Yudin,[‡] Mikhail A. Anisimov,[*,†,§] and Jan V. Sengers[†,§]

[†]Department of Chemical and Biomolecular Engineering, University of Maryland, College Park, Maryland 20742, United States

[‡]Oil and Gas Research Institute, Russian Academy of Sciences, Moscow, Russia

[§]Institute for Physical Science and Technology, University of Maryland, College Park, Maryland 20742, United States

ABSTRACT: Motivated by controversies in the literature on the microscopic and mesoscopic structure of some aqueous solutions, we have performed static and dynamic light-scattering experiments in aqueous solutions of 3-methylpyridine (3MP) and tertiary butyl alcohol (TBA). In addition to the microscopic concentration fluctuations we have found the presence of reproducible mesoscopic inhomogeneities, which become especially pronounced below room temperature. We find that the observed inhomogeneities are near-spherical Brownian aggregates of a size from a hundred to a few hundred nm. We speculate that these aggregates are long-lived metastable clathrate-like precursors triggered by minute traces of impurities in these solutions.

1. INTRODUCTION

John Prausnitz has justifiably been credited for having established molecular thermodynamics as a major chemical engineering discipline.[1−3] This approach is based on relating the macroscopic thermodynamic behavior of fluids to the microscopic molecular structures and interactions.[3,4] As Prausnitz has pointed out, molecular thermodynamics can also be extended to complex fluids in soft condensed matter[5,6] and even to aqueous protein solutions[5,7] and other biomolecular solutions.[8,9] In complex fluids often structures emerge that have a length scale much larger than the microscopic size of individual molecules.[6] Such complex fluids require an approach that in the words of Prausnitz is neither "macro, nor micro, but meso".[10]

This paper is concerned with the possible presence of mesoscale structures and inhomogeneities in aqueous solutions of small molecules or ions. As will be further elucidated in the subsequent section, the existence of such inhomogeneities has been discussed and disputed in the literature for many years, but a consensus on the subject has not yet been achieved. The spectrum of views and explanations for the observed phenomena range from structural liquid-phase transitions[11] to alleged artifacts,[12,13] from stable mesoscale "clathrate-like" colloidal particles[14] to genuine clathrate aggregation caused by impurities,[15,16] and from long-lived nonequilibrium microphase separation[17,18] to kinetically arrested gaseous nanobubbles.[19] This spectrum of opinions suggests that the investigators may be dealing with a variety of different phenomena. When we had an opportunity to discuss this issue with John Prausnitz, he reminded us that long-lived nonequilibrium states are frequently encountered in aqueous protein solutions.[20,21] We believe that a reliable knowledge of the physical and chemical parameters that control the properties of aqueous solutions will be a prerequisite for a complete understanding of aqueous biomolecular solutions.

Light-scattering techniques provide a useful tool for investigating structures in fluids at mesoscales. In Section 2 we review the literature on the possible presence of such structures in some aqueous solutions with an emphasis on the controversies concerning the observation and interpretation of results reported for aqueous solutions of 3-methylpyridine (3MP) and tertiary butyl alcohol (TBA). These controversies have motivated us to embark on performing some systematic light-scattering experiments in aqueous solutions of 3MP and of TBA. The purpose of this paper is to report on the results thus far obtained.

The paper is organized as follows. After having reviewed the available literature on the subject in Section 2, we briefly describe the experimental method in Section 3. In Section 4 we report our experimental results in an attempt to investigate the effects of temperature, concentration, change in scattering angle, and of the source of the solutes on the observed light-scattering patterns. The results are discussed in Section 5. Our tentative conclusion is that inhomogeneities at the mesoscale are indeed present in these aqueous solutions prepared with the solutes from different sources. The phenomenon is reproducible and becomes especially pronounced below room temperature. We find that these inhomogeneities are near-spherical Brownian aggregates of a size from a hundred to a few hundred nm. We speculate that the observed aggregates are long-lived metastable clathrate-like precursors triggered by minute traces of impurities in these solutions.

2. THE MYSTERY OF AQUEOUS SOLUTIONS

Aqueous solutions of small "simple" molecules such as low-molecular-weight amines or alcohols are usually considered homogeneous at the mesoscale. However, mysterious inhomogeneities of the order of a hundred nanometers to a few micrometer have been repeatedly found in such miscible fluid systems.

Special Issue: John M. Prausnitz Festschrift

Received: October 28, 2010
Accepted: December 21, 2010
Published: January 21, 2011

dx.doi.org/10.1021/je101125e | *J. Chem. Eng. Data* 2011, 56, 1238–1248

In 2000, Georgalis et al. reported a dynamic light-scattering study in which they observed submicrometer "clusters" (from (50 to 500) nm) in some aqueous electrolyte solutions.[22] In 2004, Yang et al. reported the presence of a slow relaxation mode detected by dynamic light scattering in dust-free aqueous solutions of tetrahydrofuran and 1,4-dioxane, corresponding to a correlation length of (200 to 600) nm, in addition to a fast mode corresponding to the mutual diffusion at a molecular level.[23] Two years later, Sedlák reported on an extensive static and dynamic light-scattering study of a large variety of electrolyte solutions, nonelectrolyte solutions, and mixtures of liquids (about 100 solvent−solute pairs, in particular, aqueous solutions of sodium chloride, citric and acetic acids, glucose, and ethanol).[24−26] Sedlák claimed to have found unambiguous evidence of large-scale inhomogeneities (hundreds of nanometers) in all aqueous solutions studied. Sedlák suggested using the term "domains" for these inhomogeneities as an alternative to the term "clusters", commonly used for describing molecular clustering in aqueous solutions at the microscopic scale. Sedlák also claimed that in some systems the submicrometer domains were stable, but in others the domains slowly decreased over long time intervals (weeks or even months). The formation of the domains was interpreted as a universal phenomenon caused by interactions between solute molecules via hydrogen-bond bridges formed by solvent molecules, which are themselves hydrogen bonded.

Shortly after Sedlák had published these results, Jin et al. reported a light-scattering study of aqueous solutions of tetrahydrofuran, ethanol, urea, and α-cyclodextrin.[19] They also consistently observed a slow relaxation mode, corresponding to inhomogeneities of about 100 nm in diameter. However, Jin et al. attributed this slow mode to the existence of gaseous nanobubbles stabilized by solute molecules adsorbed at the gas−water interface. Their conclusion was based on the fact that the slow mode can be eliminated by repeated filtrations (120 times) through 20 nm pore filters and regenerated by air injection. Also, Jin et al. observed slow coalescence of the nanobubbles upon the addition of salt.[27] These findings deserve serious attention, and the interpretation of the slow mode, reported so far for many aqueous solutions of nonelectrolytes, as the effect of kinetically stabilized air nano bubbles, seems plausible.

Another question discussed in the literature is whether there are inhomogeneities coupled with the well-understood concentration fluctuations diverging near the critical point of phase separation. In particular, while studying critical phenomena in a ternary system of 3MP, water, and sodium bromide by light scattering, Jacob et al. observed a very pronounced background scattering in addition to the critical opalescence.[28] The authors assumed this phenomenon to indicate the formation of a mesoheterogeneous phase, caused by clustering of neutral molecules and ions.[28,29] This interpretation was also supported by SAXS studies, which showed the presence of "clusters" in these solutions.[30] In addition, a soap-like third phase was also observed in some aqueous near-critical systems as a subtle precipitant at the liquid−liquid interface.[17] The authors attributed the formation of this phase to "coagulation of the solute driven by hydrophobic effects". However, further studies of the ternary solution of 3MP, water, and sodium bromide, such as heat-capacity measurements carried out by Van Roie et al.,[31] measurements of light scattering, liquid−liquid coexistence curves, and shear viscosity by Schröer and co-workers,[18,32−34] and coexistence curve and turbidity by Gutkowski et al.,[35] did not support the existence of any mesoscale inhomogeneities different from the diverging critical fluctuations of concentration.

In view of the controversies surrounding ternary solutions of 3MP, water, and sodium bromide, the system was revisited by Kostko et al.[36] who demonstrated that the strong background scattering previously observed by Jacob et al.[28−30] was a result of long-lived (lasting for hours) nonequilibrium inhomogeneities in the one-phase region. To better understand the origin of these inhomogeneities, Kostko et al. also studied the binary system 3MP and water without salt, which is miscible in all proportions. Three samples, namely, two samples with 0.072 mole fraction 3MP from two different sources (# 1 and # 2) and another sample with 0.082 mole fraction 3MP (from source # 2), were investigated. Dynamic light-scattering studies of these binary samples at 20 °C revealed that the time-dependent correlation function was not a single exponential but contains an additional mode, which was much slower (in the range of milliseconds) than the diffusive mode associated with the concentration fluctuations [in the range of about (30 to 50) μs]. On raising the temperature to 60 °C, where the solution comes closer to instability caused by the proximity to the virtual near-critical phase separation, the relative contribution from this slower mode decreases, while the mode associated with the relaxation of the concentration fluctuations becomes more pronounced and the time-dependent correlation function is closer to a single exponential. It was also observed that the amplitude of the slower mode was dependent on the sample source. The samples from source # 2 became very turbid after preparation and remained turbid for months. All of these observations led Kostko et al. to conclude that the energy landscape in aqueous solutions of 3MP is such that the system forms supramolecular structures which could remain stable for times longer than the times needed to conduct light-scattering experiments. They also pointed out that inducing phase separation by the addition of a salt to such systems makes the inhomogeneities less stable.[36] Long-lived nonequilibrium inhomogeneities in ternary solutions of 3MP, water, and sodium bromide were also observed by Schröer and co-workers.[18,34]

The observations in aqueous 3MP solutions are remarkably similar to those reported many years ago on aqueous TBA solutions. Light-scattering investigations in aqueous TBA solutions were first reported by Vuks and Shurupova.[11] They observed anomalous light scattering in an aqueous solution of TBA at about 0.03 mole fraction of TBA in water. They attributed this phenomenon to some kind of a "phase transition" in the liquid phase between a clathrate-like ordering and a less ordered structure. Two years later, more detailed light-scattering experiments in this system were carried out by Beer, Jr. and Jolly.[12] They noticed that the effects reported by Vuks and Shurupova are dependent on the purity of the sample and the prehistory of the sample preparation. However, they called attention to the existence of sharp maxima in the partial molar enthalpies of TBA solutions with various electrolytes and nonelectrolytes and attributed the results of Vuks and Shurupova to the formation of droplets of insoluble impurities. Soon after this, isobaric heat-capacity measurements in the same system were carried out by Anisimov et al.[37,38] who observed a line of heat-capacity maxima between 0.01 and 0.1 mole fraction TBA in water. The greatest effect was observed at about 0.075 mole fraction TBA at a temperature of about 0 °C. Anisimov et al. attributed the heat-capacity anomaly to a nanoscale structural transformation in the liquid phase but, at the same time, pointed out that the anomalous light scattering observed by Vuks and

Shurupova[11] may have been a spurious effect. They conjectured that the structural transformation should be of a short-range quasi-crystalline order and would not reach a mesoscale to cause the observed light-scattering anomaly. They further suggested that a sudden decrease in solubility of liquid impurities or gases near the line of these structural transformations could produce nanosize droplets or bubbles which might cause anomalous light scattering. Later experiments carried out by Euliss and Sorensen showed that in an aqueous TBA solution, at a concentration of 0.07 mole fraction TBA, stable submicrometer particles (about 100 nm size) appeared below room temperature.[15] These particles disappeared upon heating to room temperature. Even after double distilling the TBA and redistilling the water in quartz still, these particles persisted. These observations led Euliss and Sorensen to speculate that the effect "might be related to some stable solid clathrate of tert-butanol in water perhaps involving a trace help gas to promote stability". Subsequent light-scattering studies in aqueous TBA solutions were also carried out by Bender and Pecora,[13] but their experiments did not show any anomalous light scattering. On the other hand, Bender and Pecora did observe mysterious submicrometer particles in aqueous solutions of 2-butoxyethanol (2BE) below 0.02 mole fraction 2BE.[16] However, the phenomenon was strongly dependent on the source of 2BE, forcing Bender and Pecora to conclude that small amounts of undetectable impurities might be responsible for the anomaly. Another system, which shows similar behavior, is the aqueous solution of tetrahydrofuran (THF).[39] Remarkably, the aqueous solutions of 3MP, TBA, 2BE, and THF share two common features: with addition of a third component they all form mixed clathrates in solid phases[39−42] and exhibit closed-loop phase separation in the liquid phase upon the addition of salts.[15,36,43,44]

Thus the origin of meso-heterogeneities observed in aqueous solutions still remains unclear. Motivated by the controversies about the microscopic and mesoscopic structure of aqueous solutions, we have embarked on some systematic light-scattering experiments in aqueous solutions of 3MP and TBA in an attempt to understand the effects of temperature, concentration, change in the scattering angle, and source of the solutes. We find anomalous light scattering at low temperatures in both of these systems regardless of the source. The effect is reproducible. The light scattering becomes enhanced at temperatures below room temperature and decreases as the temperature is raised. The time-dependent correlation functions always show the presence of two relaxation modes: the anticipated and well-understood molecular-diffusion mode and a slower "mesoscale" mode corresponding to the decay time of the order of milliseconds, also diffusive in nature. The faster mode in TBA solutions, associated with the diffusive relaxation of the concentration fluctuations, is in agreement with the results reported by Euliss and Sorensen[15] and Bender and Pecora.[13] The "mesoscale" mode, associated with Brownian motion of near-spherical particles with an average hydrodynamic radius from a hundred to a few hundred nm, becomes dominant below room temperature. In addition to these two diffusive modes, a broad distribution of much larger inhomogeneities [order of (10 to 100) μm], probably resulting from partial aggregation of the observed submicrometer particles, is also seen in a long-time tail of the correlation function. The nature and origin of the "mesoscale particles" are very puzzling, and while we still do not have a complete answer, we believe they are metastable aggregates originating from the intrinsic structure of aqueous solutions, even if their emergence is triggered by traces of impurities.

3. EXPERIMENTAL METHOD AND PROCEDURE

3.1. Sample Preparation. Three aqueous solutions with 0.071, 0.072, and 0.312 mole fraction 3MP were prepared with a 3MP sample (declared purity 0.995+) obtained from Sigma Aldrich. The 3MP was used without further purification. The water was filtered through a 20 nm filter.

For the investigation of aqueous TBA solutions, two sources of TBA were used: one from Sigma Aldrich with a purity of 0.997+ and another one from Alfa Aesar with a purity of 0.998+. One sample with 0.083 mole fraction TBA was prepared by using the TBA from Sigma Aldrich. Other aqueous samples with 0.010, 0.040, 0.073, 0.087, and 0.110 mole fraction TBA were prepared by using TBA from Alfa Aesar. The optical cells were first washed and rinsed with dust-free water and ethanol, and then dried with dust-free nitrogen gas. The dust-free nitrogen gas was of high-purity (HP) grade, purchased from Airgas. Water (from a Millipore setup) and TBA were initially filtered 2 to 3 times with a 200 nm polypropylene hydrophilic filter. Each sample was first checked visually for the presence of any dust particles in the propagating laser beam. Additional filtrations were carried until we verified that no sudden spikes would appear in the scattered intensity. All of the samples, with the exceptions of those with 0.040, 0.073, and 0.087 mole fraction TBA, were covered with a Teflon tape (previously washed with dust-free water and ethanol and dried using HP nitrogen gas) and sealed with polyethylene glue. The remaining samples with 0.040, 0.073, and 0.087 mole fraction TBA were flame-sealed.

3.2. Light-Scattering Technique and Procedure. The light-scattering experiments in aqueous 3MP solutions were carried out with the same custom-made setup used previously in our laboratory.[36,45−47] The optical arrangement enables simultaneous measurements of the light scattered at two different scattering angles by alternating between two different incident He−Ne laser beams (10 mW) as described by Jacob et al.[45] Both the intensity of the scattered light and its time-dependent correlation function were determined.

The sequence of measurements was as follows: The sample was allowed to equilibrate for a period of 50 min. During the next 10 min, the scattering intensity from one laser was recorded, while the second laser remained closed by a shutter. Subsequently, the first shutter was closed and the second shutter operated in the same sequence to measure the scattering intensity from the second laser. Each run thus yielded light-scattering data corresponding to two different scattering angles.[45] A total of 24 such runs were performed over a total experimental time of about 24 h. Experiments were carried out at temperatures in the range from (3 to 85) °C. The temperature stability, provided by a precision programmable thermostat used for the light-scattering measurements in polymer and 3MP solutions,[36,45−47] was better than ± 0.01 °C. The time-dependent correlation functions in homodyne mode were obtained by using an ALV-5000 correlator.

The light-scattering experiments in aqueous TBA solutions were carried out with a different light-scattering setup supplied by Photocor Instruments. This setup consisted of a single He−Ne laser, a single photomultiplier, and an automatic goniometer. The optical cell with the aqueous TBA sample was submerged in a liquid (silicone oil with a refractive index of 1.498 that closely matches the refractive index of the optical cell) to obtain a uniform temperature around the sample and to avoid any stray light. The sample was subjected to various temperatures ranging from (8 to 50) °C, with a temperature control better than ± 0.1 °C. The thermostat consists of an electric heater and a water cooler which are part of the Photocor light-scattering setup. The heating rate was about 8 $°C \cdot h^{-1}$, while the cooling rate was about 5 $°C \cdot h^{-1}$. At each temperature, the sample was allowed to equilibrate for about 2 h before taking a reading. The scattering angles were varied from 20° to 135°. The time-dependent autocorrelation function in the homodyne mode was obtained by using a Photocor correlator. An option in Photocor software was used to eliminate the effect of occasional spikes seen in the intensity caused by large (> 10 μm) aggregates. In this software the total accumulation time is broken down into small segments [of the order of (30 to 60) s]. After all segments of the correlation function are collected, the program disregards any segments during which the scattering intensity spiked beyond a preset limit and then computes the correlation function based on the remaining segments.

The intensity auto-correlation function $g_2(t)$ for a single-exponential relaxation mode is given by[48]

$$g_2(t) - 1 = A \exp(-2\Gamma t) \tag{1}$$

where A is the amplitude, t is the lag time, and Γ is the decay rate related to the relaxation time τ of the fluctuations by $\Gamma = 1/\tau$. If the relaxation time is associated with diffusion of molecules or particles, then the decay rate is:

$$\Gamma = Dq^2 \tag{2}$$

where $q = (4\pi n/\lambda)\sin(\theta/2)$ is the wavenumber (n is the refractive index of the scattering medium, λ is the wavelength of the laser beam, and θ is the scattering angle) and D is the translational diffusion coefficient. For Brownian monodisperse spherical noninteractive particles,[48]

$$D = \frac{k_B T}{6\pi\eta R} \tag{3}$$

where k_B is Boltzmann's constant, T is the temperature, η is the shear viscosity of the medium, and R is the hydrodynamic radius of the particles.

The reliability of the first light-scattering setup used for the aqueous solutions of 3MP was tested by observing the light scattered from an aqueous solution of latex particles and confirming the presence of a simple exponential diffusive decay in the aqueous solution of latex particles. The reliability of the second light-scattering setup used for the aqueous solutions of TBA, was tested by measuring both static and dynamic light scattering in a 0.5 mass fraction binary solution of hexane and toluene at 25 °C. The light-scattering intensity in the range of the scattering angles θ = 30° to 135° was found to be symmetric around 90° to within 4 % deviation.[49] From the time-dependent correlation function only the molecular diffusion mode was detected. The mutual diffusion coefficient was obtained as $(2.9 \pm 0.3) \cdot 10^{-5}$ $cm^2 \cdot s^{-1}$, which agrees with the value $2.757 \cdot 10^{-5}$ $cm^2 \cdot s^{-1}$ quoted by Segrè et al.[50]

4. EXPERIMENTAL RESULTS

4.1. Aqueous Solutions of 3-Methylpyridine. 3MP and water are miscible in all proportions. However, the overall light-scattering intensity increases upon heating from room temperature and reaches a maximum at about 75 °C where the system is close to a virtual critical instability (Figure 1). Around this temperature a small addition of salt, such as NaCl or NaBr, causes a closed-loop phase separation with upper and lower critical points.[36] Near the instability, the concentration fluctuations dominate the static and dynamic light scattering, but upon cooling they become weaker and faster, respectively. We confirmed the findings reported by Kostko et al.,[36] namely, that the correlation function is close to a single exponential only at high temperatures above 60 °C, while upon cooling another, much slower ("mesoscale") mode emerges and dominates below room temperature. The relaxation times of these two modes as functions of temperature are shown in Figures 2 and 3. As the aqueous samples with 0.071 and 0.312 mole fraction 3MP were cooled down from 30 °C to 5 °C, it was observed that the relaxation time of the mesoscale mode increased by an order of magnitude to tens of milliseconds. The temperature dependence of the relaxation time τ_1 of the molecular mode follows the trend

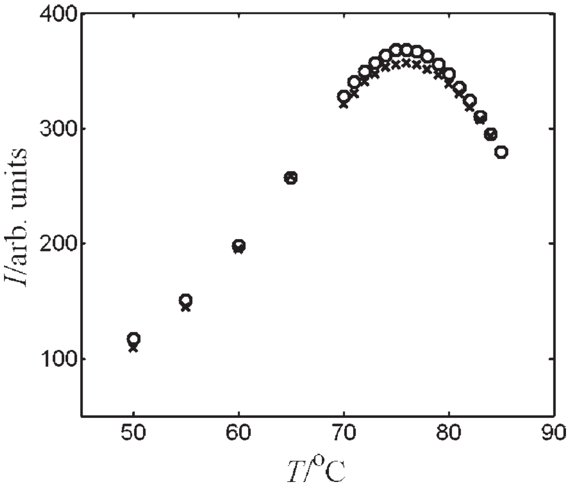

Figure 1. Light-scattering intensity of the 0.072 mole fraction 3MP aqueous solution at a scattering angle θ = 45° as a function of temperature. Circles indicate the intensity data upon heating from (50 to 85) °C, and crosses indicate intensity data upon cooling from (85 to 50) °C. The maximum intensity is observed at about 75 °C where the system is close to a virtual critical instability.

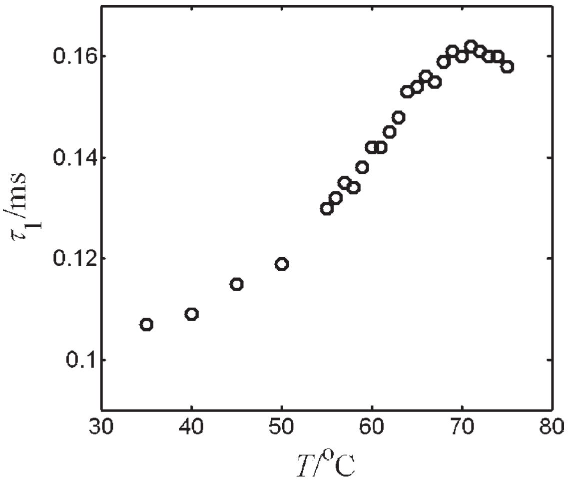

Figure 2. Relaxation time τ_1 of the molecular diffusion mode in the 0.072 mole fraction 3MP aqueous solution at a scattering angle θ = 45° as a function of temperature.

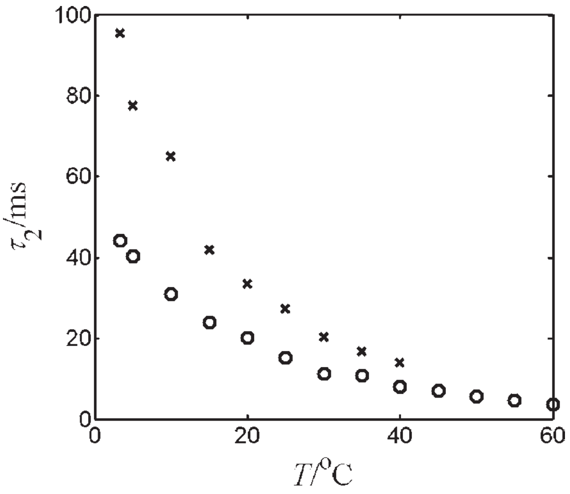

Figure 3. Relaxation time τ_2 of the mesoscale dynamic mode in 3MP aqueous solutions at a scattering angle $\theta = 45°$ as a function of temperature. Circles correspond to the 0.072 mole fraction 3MP aqueous solution and crosses to the 0.312 mole fraction 3MP aqueous solution.

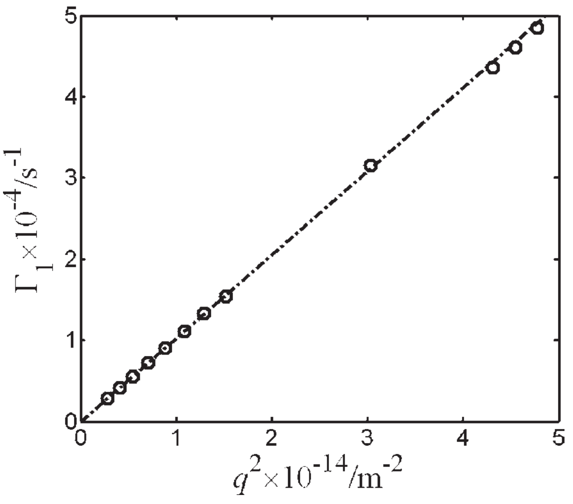

Figure 4. Wavenumber dependence of the decay rate Γ_1 of the molecular diffusion mode in the 0.072 mole fraction 3MP aqueous solution at 25 °C. The slope of the line yields the diffusion coefficient $D = 1.0 \cdot 10^{-6}$ cm$^2 \cdot$s^{-1} in accordance with eq 2.

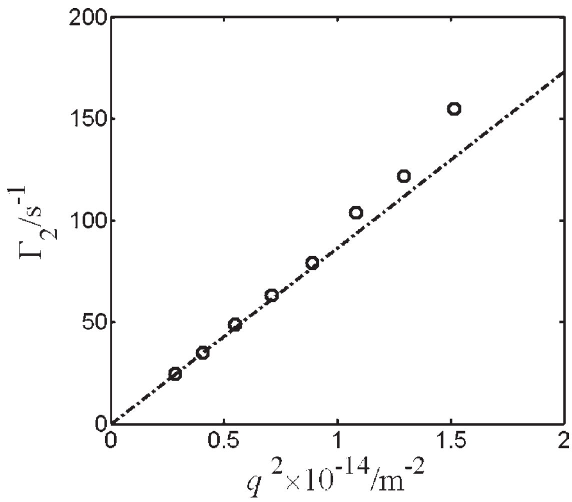

Figure 5. Wavenumber dependence of the decay rate Γ_2 of the mesoscale diffusion mode in the 0.072 mole fraction 3MP aqueous solution at 25 °C. The initial slope yields a diffusion coefficient $D = 8.6 \cdot 10^{-9}$ cm$^2 \cdot$s^{-1} in accordance with eq 2. The deviation from linearity at larger wave numbers is attributed to polydispersity of the mesoscale particles.

in the scattered intensity. The temperature dependence of the relaxation time τ_2 for the mesoscale mode follows the temperature dependence of the viscosity of aqueous 3MP solutions and increases strongly upon cooling.[51] Both the molecular mode and the mesoscale mode correspond to diffusion dynamics: as illustrated by Figures 4 and 5, with the decay rates Γ_1 and Γ_2 being proportional to the square of the wavenumber in agreement with eq 2. This fact is obvious for the molecular mode associated with the diffusive relaxation of the concentration fluctuations. The refractive index data needed here for 3MP aqueous solutions were taken from ref 36, where we assumed that the equation can be extrapolated to zero salt concentration. For the mesoscale mode, the validity of eq 2 implies Brownian diffusion of particles with a size greater than the correlation length of the concentration fluctuations by 2 orders of magnitude. As seen from Figure 5, eq 2 describes the data accurately only for small wavenumbers. At larger wave numbers, the effective slope of Γ_2 versus q^2 is larger. This phenomenon indicates polydispersity of the mesoscale particles: the contribution from smaller particles is more pronounced at larger scattering angles. While the molecular diffusion mode becomes faster upon cooling (Figure 2), the mesoscale mode becomes slower upon cooling (Figure 3). We have also found that the relaxation time τ_2 of the mesoscale mode for a sample with 0.071 mole fraction 3MP was smaller than for a sample with 0.312 mole fraction 3MP (Figure 3), as expected from the increase of the viscosity with an increase of 3MP concentration.[51]

Using accurate viscosity data reported for aqueous 3MP solutions by Wang et al.,[51] we calculated the average hydrodynamic radius of the particles responsible for the mesoscale mode with the aid of eq 3. The average size of the observed particles varies from about 200 nm at 40 °C to about 300 nm at about 3 °C for both samples, with 0.071 and with 0.312 mole fraction 3MP (Figure 6). The temperature dependence of the particle size for the mesoscale diffusion is less significant than the temperature dependence of viscosity, which appears to be the major cause for the dramatic increase of the "mesoscale" relaxation time upon cooling, as demonstrated in Figure 3.

In addition to the two diffusive modes, "molecular" and "mesoscale", we have also observed a very slow third mode (order of seconds) which is not visible at high temperatures around or above 60 °C but can be seen at lower temperatures. The decay rate of this mode shows no clear q^2 dependence and is most likely associated with large multimicrometer aggregates of the particles. The sharp "spikes" in the light-scattering intensity are attributed to these large inhomogeneities. The number of such inhomogeneities in the scattering volume is too small to apply a statistical treatment of the resulting long-time tail in the correlation function.

4.2. Solutions of *tert*-Butyl Alcohol.

In the search for understanding the nature of mesoscopic inhomogeneities in aqueous solutions, solutions of TBA in water occupy a special place. The hydroxyl group of a TBA molecule and its hydrocarbon part perfectly balance the amphiphilic nature of the molecule.[52,53]

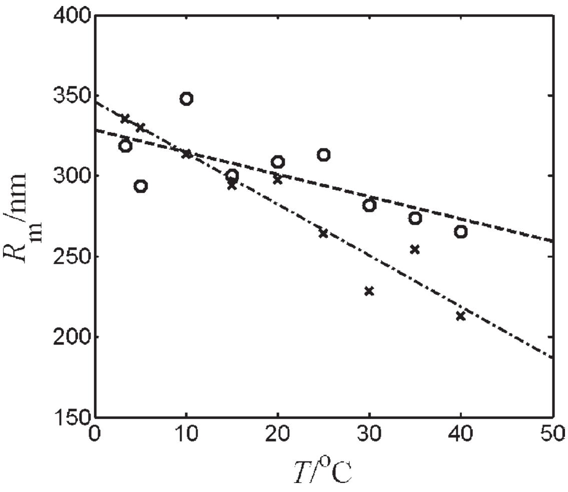

Figure 6. Effective hydrodynamic radius R_m of the mesoscale particles in 3MP aqueous solutions at a scattering angle $\theta = 45°$ as a function of temperature. Circles correspond to the 0.072 mole fraction 3MP aqueous solution and crosses to the 0.312 mole fraction 3MP aqueous solution. The dashed line shows the particle-size trend in the 0.072 mole fraction 3MP aqueous solution and the dotted-dashed line the particle-size trend in the 0.312 mole fraction 3MP aqueous solution.

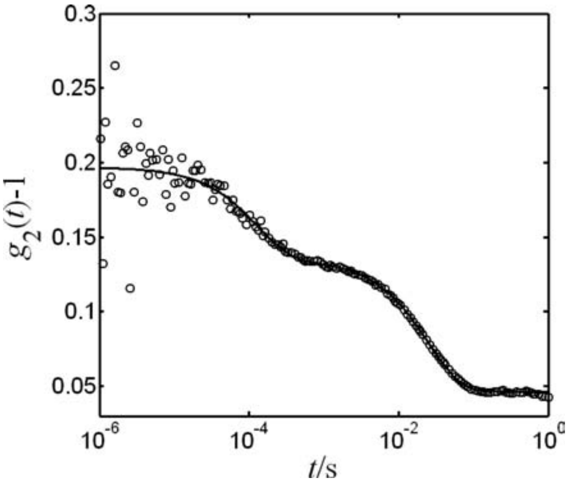

Figure 7. Time-dependent correlation function (open circles) for the 0.083 mole fraction TBA aqueous solution at a scattering angle $\theta = 30°$ obtained at $T = 22.8$ °C. The solid curve represents a fit of the data to two exponential decays with two decay times corresponding to the molecular diffusion ($D = 1.5 \cdot 10^{-6}$ cm$^2 \cdot$s^{-1}) and the mesoscale diffusion ($D = 4.2 \cdot 10^{-9}$ cm$^2 \cdot$s^{-1}), respectively. An additional long-time tail of the dynamic correlation function is assumed to be a background contribution.

Moreover, the *tert*-butyl group fits seamlessly into the spherical cavity of the cage structure in water. TBA, similarly to 3MP, is also miscible with water in all proportions. However, unlike 3MP, the TBA solutions at ambient conditions are far away from liquid−liquid immiscibility, and the relaxation of concentration fluctuations is relatively fast. Regarding the molecular and supramolecular structure of aqueous TBA solutions, many experiments and computer simulations indicate some clustering on the scale of a nanometer.[52−67] In spite of some speculation that can be found in the literature,[53,65] such molecular clustering cannot be directly observed by dynamic light scattering as clearly shown in refs 13 and 15 since it cannot cause significant fluctuations of the refractive index.

We have detected the molecular diffusion mode in TBA solutions, which is consistent with the previously published results of Euliss and Sorensen[15] and Bender and Pecora.[13] The molecular diffusion mode at room temperature corresponds to a relaxation time of the order of 10 μs at the scattering angle $\theta = 30°$ ($q = 6.96 \cdot 10^6$ m^{-1}) in accordance with eqs 1 and 2. The refractive-index data of aqueous TBA solutions needed for determining the scattering wavenumber were taken from the literature.[53] We have calculated the "radius" (the correlation length) of the concentration fluctuations by using eq 3. For example, for the 0.083 mole fraction TBA aqueous solution at 22.8 °C, this "radius" is (0.4 ± 0.1) nm. This result is in good agreement with the value of 0.4 nm reported by Euliss and Sorensen for an aqueous solution of the TBA mole fraction of 0.073 at 20 °C. The viscosity data for aqueous TBA solutions, used here, were measured by Euliss and Sorensen[15] with dynamic light scattering by embedding calibrated latex particles in the solution. In addition, at room temperatures [(21 to 23) °C], the correlation function shows the presence of a mesoscale relaxation mode (order of a millisecond at $\theta = 30°$) and a contribution from much slower inhomogeneities with a decay time of the order of seconds, similarly to what was observed in 3MP solutions (Figure 7). We have confirmed that these inhomogeneities are associated with sharp spikes in the light-scattering intensity previously reported by Kostko et al.[36] By using the Photocor "dust cut-off" software we were able to reduce or completely eliminate the contribution from the intensity spikes, such that the long-time tail of the correlation function would practically disappear. The correlation function, obtained at room temperature for a sample with 0.083 mole fraction TBA at $\theta = 30°$ with a preset spike-tolerance limit of 100 %, is shown in Figure 7. The remaining segments are 19 % of the totally accumulated correlation function. As seen from the fit of the correlation function to two exponentials, two distinct relaxation modes are present, the molecular diffusion mode and a mesoscale mode, separated by two orders of magnitude in their decay times. The long-time tail of the correlation function, which corresponds to a decay time longer than a second, has been treated as a background fitting parameter.

Upon cooling below room temperature, a significant increase in intensity is observed. The intensity increased up to two orders in magnitude, as seen in Figure 8. We heated the sample from 8 °C up to 50 °C and then cooled it back to 8 °C. This cycle was repeated several times. We always observed an increase of the light-scattering intensity, an increase of the amplitude of the mesoscale mode upon cooling, and a virtual disappearance of this effect upon heating well below room temperatures. Thus this effect is reproducible. We also repeated the cycle after additionally filtering the sample with a 200 nm filter at room temperature. This filtration did not have any significant effect on the observed anomaly. The sample was also left undisturbed for five days at 15 °C. During this period the light-scattering intensity remained relatively stable.

The correlation function, obtained for the sample with 0.083 mole fraction TBA at $\theta = 30°$ and at 8.5 °C, is shown in Figure 9. The fit of the correlation function to a single exponential decay corresponds to a pronounced mesoscale mode. Contributions from the molecular scattering and from large (> 10 μm) inhomogeneities become insignificant.

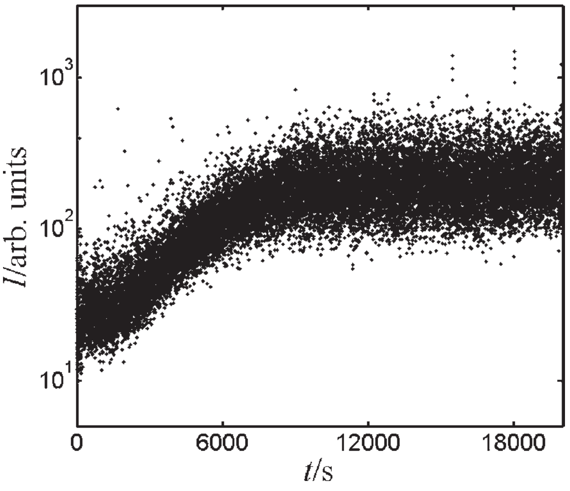

Figure 8. Time evolution of the light-scattering intensity upon cooling from (50 to 8) °C for the 0.087 mole fraction TBA aqueous solution at a scattering angle $\theta = 45°$.

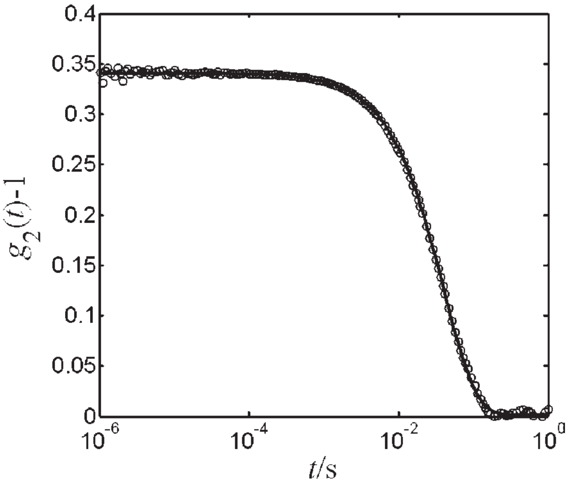

Figure 9. Time-dependent correlation function (open circles) for the 0.083 mole fraction TBA aqueous solution at $T = 8.5$ °C and a scattering angle $\theta = 60°$. The solid curve represents the fit to a single exponential decay. This fit approximates the mesoscale mode as being associated with Brownian diffusion ($D = 6.9 \cdot 10^{-10}$ cm$^2 \cdot$s^{-1}) of monodisperse particles, which actually display some polydispersity.

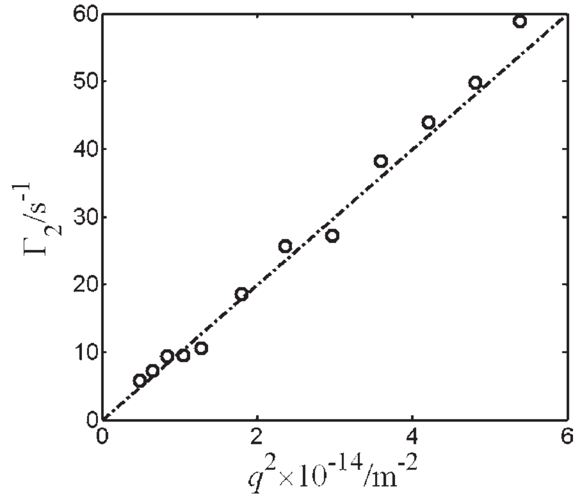

Figure 10. Wavenumber dependence of the decay rate Γ_2 of the mesoscale mode in the 0.083 mole fraction TBA aqueous solution at $T = 20.8$ °C. The slope of the linear dependence yields the average effective diffusion coefficient ($D \simeq 1.0 \cdot 10^{-9}$ cm$^2 \cdot$s^{-1}).

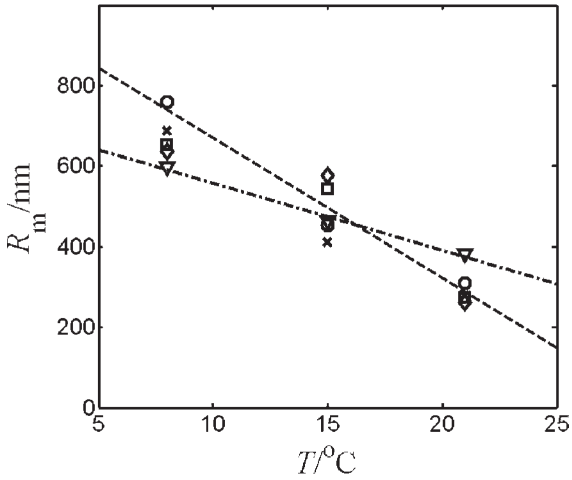

Figure 11. Effective hydrodynamic radius R_m of the mesoscale particles as a function of temperature for the 0.083 mole fraction TBA aqueous solution. ○, $\theta = 20°$; ×, $\theta = 30°$; □, $\theta = 45°$; ◇, $\theta = 60°$; △, $\theta = 90°$. The dashed line shows the trend of the temperature dependence of the particle size obtained from scattering at $\theta = 20°$ and the dotted-dashed line the trend of the particle size obtained from scattering at $\theta = 90°$. The steeper slope is attributed to particle polydispersity.

We have measured the decay rate of the mesoscale mode at various scattering angles. As seen from Figure 10, the mesoscale mode in the TBA solutions obeys, within the experimental errors, simple diffusion dynamics described by eq 2. We have calculated an average hydrodynamic radius R_m associated with the mesoscale mode by using eq 3. The average size of the observed particles for the 0.073 mole fraction TBA aqueous solution varies from about 300 nm at 21 °C to about 800 nm at about 8 °C (Figure 11). If these particles were monodisperse, one would expect that the particle size, at a particular temperature, should remain constant when probed with different angles. However, it is seen in Figure 11 that there is a certain discrepancy in the particle size measured at different angles at a given temperature. Thus we conclude that these particles are generally polydisperse. The polydispersity increases upon cooling. This conclusion is supported by the fact that at 8 °C the effective particle sizes obtained for small angles ($\theta = 20°$ and $\theta = 30°$) are largest, because larger particles scatter more light at smaller angles.

We have also measured the overall light-scattering intensity at various scattering angles ranging from 20° to 135°. The angular distribution exhibits a strong asymmetry, which becomes even more pronounced at low temperatures (Figure 12), where the inverse intensity approximately follows a q^2 dependence with the slope given by $(1/3)R_g^2/I(q = 0)$ where R_g is the average radius of gyration and $I(q = 0)$ is the intensity extrapolated to zero wavenumber;[48] the effect is consistent with the results obtained from the correlation-function analysis (Figure 10). The scattered intensity depolarization ratio at the angle of 90° has also been measured. This ratio is very close to zero. We thus conclude that the shape of the particles associated with the mesoscale

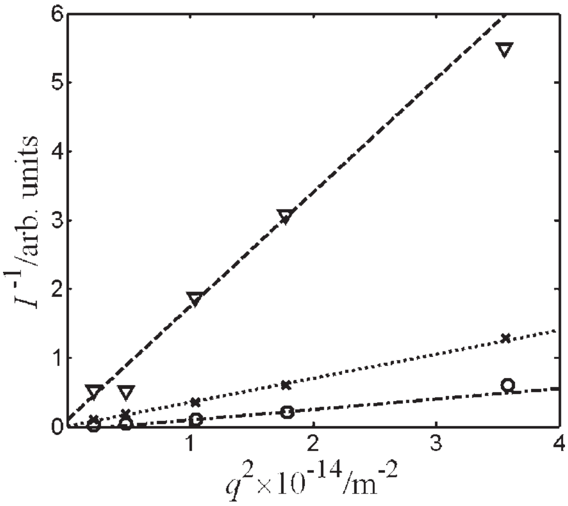

Figure 12. Wavenumber dependence of the inverse light-scattering intensity for the 0.073 mole fraction TBA aqueous solution. ○, T = 8.5 °C; ×, T = 21 °C; △, T = 50 °C. The straight lines are given for guidance.

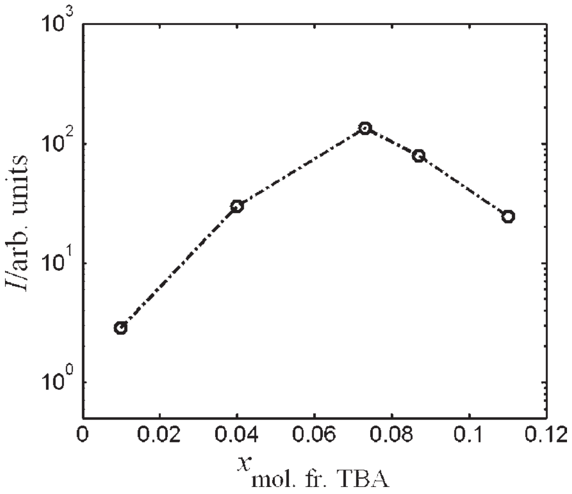

Figure 13. Light-scattering intensity in the aqueous solution with different mole fractions of TBA at a scattering angle θ = 45° and at T = 8.5 °C.

mode is nearly spherical, as the anisotropic contribution in the light-scattering intensity is negligible.

We have performed similar experiments with samples prepared from the second source of TBA (Alfa Aesar). Samples with concentration from 0.01 to 0.11 mole fraction TBA were tested. A maximum in the light-scattering intensity has been observed for the 0.073 mole fraction TBA solution (8.5 °C) and a scattering angle θ = 45° (Figure 13). At all concentrations the molecular diffusion mode was detected. The angular distribution of the scattering intensity exhibits a strong asymmetry associated with the presence of mesoscale particles.

We were able to clearly detect the mesoscale relaxation mode for all concentrations investigated. The mesoscale mode became highly pronounced at lower temperatures. The average size of the observed mesoscale particles, for various concentrations at 8.5 °C, varies from about 150 nm to about 400 nm depending on the wavenumber probed. A larger effective size is observed at smaller angles; this effect can be attributed to the polydispersity of these particles. Therefore, the mesoscale particles are equally formed in solutions prepared from different sources of TBA, although the average size under the same conditions is not exactly the same.

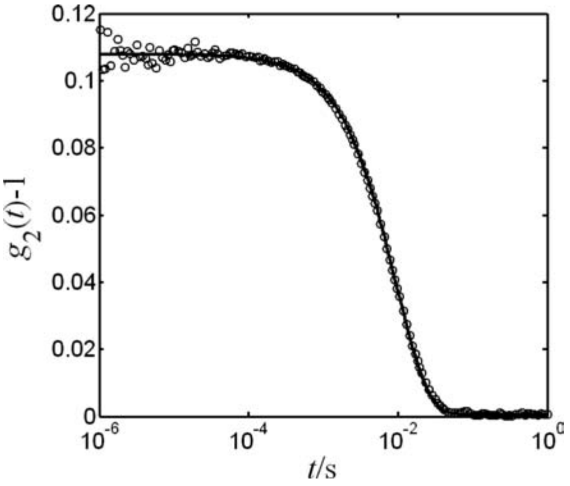

Figure 14. Time-dependent correlation function (open circles) for the 0.073 mole fraction TBA aqueous solution at a scattering angle θ = 60° and at T = 8.5 °C, obtained after fast cooling of the sample. The solid curve represents a fit to a single exponential decay. This fit approximates the mesoscale mode as being associated with Brownian diffusion (D = $3.0 \cdot 10^{-9}$ cm$^2 \cdot$s^{-1}) of monodisperse particles. In this case the mesoscale particles are smaller and exhibit less polydispersity as compared to that observed in Figure 10.

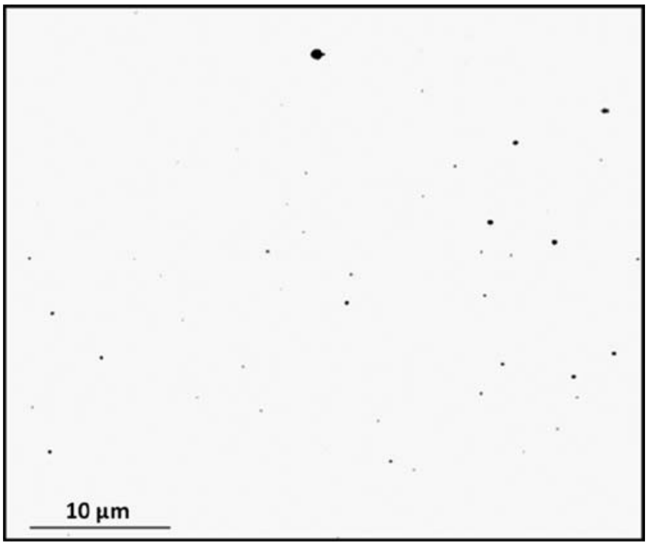

Figure 15. Confocal microscopy images of the 0.083 mole fraction TBA aqueous solution at about 10 °C. The particles are polydisperse and range in size from a few hundred nanometers to a micrometer.

Some preliminary experiments were also carried out by fast cooling (7 °C·min^{-1}) from (50 to 8.5) °C of the sample with 0.073 mole fraction TBA. The sample was then left to "equilibrate" for two hours. The mesoscale particles formed in this sample appear somewhat different from those formed in the slowly cooled (5 °C·h^{-1}) sample. As seen in Figure 14, the correlation function can be nicely fitted to a single exponential without showing any significant polydispersity of the mesoscale particles. Moreover, the particle size is smaller (about 100 nm).

We monitored the correlation function for several days and did not notice a significant change of this size upon time; this fact reflects the high stability of the mesoscale aggregates in this solution.

4.3. Confocal Microscopy. To further study the mesoscale particles in the aqueous TBA solutions, we have performed some confocal microscopy experiments. The sample with 0.083 mole fraction TBA, prepared earlier for the light-scattering experiments, was studied. The confocal microscopy unit and the sample holder cell were maintained at cold temperatures by the use of ice. While the sample was at low temperatures (about 10 °C), a drop of the sample was transferred by a syringe from the optical glass vial into the sample holder. The mesoscale Brownian particles are clearly seen under the confocal microscope (Figure 15). These particles are stable only at low temperatures: as the temperature is increased, they disappear. The confocal nature of these images tells us that these particles are not of uniform size, but they range in size from a hundred nanometers to a micrometer. These observations are consistent with what is observed from light-scattering experiments.

5. DISCUSSION

We find that the mesoscopic properties of 3MP and TBA aqueous solutions are similar. In both cases, there is a detectable molecular diffusion mode associated with the concentration fluctuations. In addition, a mesoscale diffusion mode, manifested by a pronounced increase in light-scattering intensity upon cooling, is detected. We have shown that the mesoscale mode is associated with mesoscale Brownian particles, which have a near-spherical shape and a polydisperse size distribution between a hundred and a few hundred nm. Some larger inhomogeneities ($> 10\ \mu$m) are also detected, possibly caused by partial aggregation of the mesoscale particles.

The nature and the origin of the mesoscale particles are still not fully understood. However, some preliminary conclusions can be drawn from an experiment in which we filtered the sample with 0.083 mole fraction TBA through a 20 nm filter (Anopore) at a temperature below 10 °C. After filtration, the light-scattering intensity in the sample was dramatically reduced to the level typical for ordinary molecular solutions. The mesoscale mode was hardly detectable. We monitored the sample for about two days but did not detect any mesoscale particles. The refractive index of the solution after the cold filtration remained unchanged, so the filtration did not significantly change the TBA concentration.

This leads us to conclude that the observed mesoscale particles are not associated with the presence of an equilibrium meso-heterogeneous phase in the TBA and 3MP aqueous solutions. Rather, this phenomenon can be attributed to nontrivial interactions of some impurity molecules, initially present in the solution, and the fluctuations of short-ranged clathrate-like structures.[68] The clathrate-like structures refer to the short-lived liquid cavities in water structure and not to a solid-clathrate phase.[69] The impurities could be soluble gases (like air) or traces of other substances. We carried out gas chromatography of TBA obtained from the two different sources. The results show the presence of some impurity in the order of 0.001 mass fraction in the TBA supplied by Aldrich, which is consistent with the declared purity (0.997+) of the sample. The level of impurity in the TBA supplied by Alfa-Aesar (declared purity 0.998+) was undetectable. Our conclusion, in principle, is similar to the explanations proposed earlier by Euliss and Sorensen[15] and Bender and Pecora.[13]

However, we conclude that the occurrence of the mesoscale particles in aqueous solutions studied in this work is not due to the presence of gas bubbles, as shown by Jin et al.[19] for some other aqueous systems. Rather our observations are similar to those when globular aggregates are present.[70] If the observed particles were merely gaseous nanobubbles, then they should disappear when the sample is heated up and would not reappear when the sample is cooled down. Moreover, there would be no distinct onset temperature at which the avalanche-like formation of the mesoscale aggregates starts. Currently, we are planning to investigate a possible interaction of the mesoscale mode observed in TBA solutions with saturated gas in the solution.

Thus, the question arises: how can such small amount of impurities, virtually undetectable, trigger the formation of mesoscale aggregates? We suggest the following explanation. TBA and 3MP without impurities do not form solid-state clathrates.[42,71] Their aqueous solutions are not supersaturated above the crystallization temperatures. For example, the near-eutectic crystallization temperature of the 0.07 mole fraction TBA aqueous solution is about −5 °C.[72] However, it is commonly accepted that a short-ranged clathrate-like structure exists in the stable liquid phase of TBA aqueous solutions with a certain stoichiometric ratio, possibly 1 TBA/15 H_2O.[53,58] These structures exhibit fluctuations in size and geometry. However, they are, generally, short-lived and short-ranged in the stable solution. In particular, thermodynamic anomalies in the molar volume and heat capacity are attributed to the formation of these short-range clathrate-like structures.[12,37] Although these structural fluctuations may become more pronounced at the solution concentration close to the stoichiometric ratio,[53,58,65] they are too small and too short to cause any anomaly in light scattering.

The situation may become different in the presence of traces of impurities if the solute molecules form so-called “double” or mixed clathrate compounds which stoichiometrically include the impurity molecules. It is known, for example, that TBA form solid clathrate-hydrates with H_2S in the form 1 TBA/2 H_2S/17 H_2O.[42] TBA is derived commercially from isobutane as a coproduct of production of propylene oxide, which is known as a hydrate former.[69] It is possible that TBA forms solid clathrate-hydrates with other substances, such as propylene oxide, present in small amounts in the sample as impurities. Around room temperature, the solution becomes supersaturated with respect to the formation of the mixed clathrate-hydrate aggregates. The amount of the mixed-clathrate-hydrate phase is very small, as it is limited by the amount of impurities. For example, if the impurity (I) concentration in TBA is about 100 ppm, the formation of 1 TBA/2 I/17 H_2O mixed clathrates would involve a very small amount of TBA and water molecules, about 1000 ppm. By removing the mesoscale clathrate particles by filtration through a 20 nm filter at cold temperature, the source of the aggregation is eliminated, but the solution concentration and all other properties remain unchanged. For example, in a typical scattering volume of 0.01 mm^3, we roughly estimate the amount of 300 nm radius aggregates to be about 1000, along with occasional micrometer-sized particles. We are planning to test this hypothesis by adding specific impurities into the system.

It is remarkable that the mesoscale particles remain relatively stable for a long time, forming apparently a metastable colloid (“meso-heterogeneous phase”). As discussed in the previous section, this “phase” is especially stable and relatively monodisperse if the solution is cooled fast. The existence of long-lived amorphous precursors in the nucleation of clathrate hydrates from a supersaturated solution has been recently found in molecular dynamics simulations of Jacobson et al.[68] According to this study, "at low temperatures, the system can be arrested in the metastable amorphous clathrate state for times sufficiently long to appear as an intermediate state". It seems plausible that the mesoscale particles observed in the TBA and 3MP solutions are kinetically arrested amorphous precursors of mixed clathrates. The existence of a long-lived clathrate colloid formed at near-ambient temperatures from a simple aqueous solution may have promising applications in biology and engineering.

There is another implication of the specific response to impurities of the aqueous solutions like 3MP, TBA, or 2BE. It has been found that the addition of small amounts of amphiphilic ("antagonistic) salts to aqueous 2BE and 3MP solutions may result in the formation of mesophases, namely, mixed micelles in 2BE[14] and a multilamellar mesophase with an onion-like structure in 3MP.[73] We expect a similar response to the addition of an amphiphilic salt in TBA solutions and plan to test this hypothesis.

AUTHOR INFORMATION

Corresponding Author

*E-mail: anisimov@umd.edu. Tel.: +1-301-405-8049. Fax: +1-301-314-9404.

Present Addresses

⊥School of Science and Engineering, Reykjavik University, Menntavegur 1, 101 Reykjavík, Iceland.

Funding Sources

This research is supported by the Division of Chemistry of the National Science Foundation (Grant No. CHE-1012052). An acknowledgment is also made to the donors of the ACS Petroleum Research Fund for the support of D. A. Ivanov during his stay at the University of Maryland, College Park.

ACKNOWLEDGMENT

We have appreciated useful discussions with C. M. Sorensen, T. M. Bender, R. Pecora, and C. Peters. We are indebted to D. Blair and his research group at Georgetown University for letting us use their confocal microscope and to I. Kipnis and his staff at the Department of Chemistry and Biochemistry, University of Maryland, College Park, for letting us use gas chromatography. We also thank A. F. Kostko for his advice on the experiments with 3MP and A. Trubetskaya, Y. Liu, and B. Katoski for helping us with sample preparations.

REFERENCES

(1) Knapp, H.; Sandler, S. I. A short history of molecular thermodynamics and a tribute to John M. Prausnitz. *Ind. Eng. Chem.* **1998**, *37*, 2899–2902.

(2) O'Connell, J. P.; Cummins, P. T. John M. Prausnitz at Berkeley, 1955−2005. *Fluid Phase Equilib.* **2006**, *24*, 1–3.

(3) Prausnitz, J. M. *Molecular Thermodynamics of Fluid-Phase Equilibria*; Prentice-Hall: Englewood Cliffs, NJ, 1969.

(4) Prausnitz, J. M.; Lichtenthaler, R. N.; Gomes de Azevedo, E. *Molecular Thermodynamics of Fluid-Phase Equilibria*, 3rd ed.; Prentice-Hall: Upper Saddle River, NJ, 1999.

(5) Prausnitz, J. M. Some new frontiers in chemical engineering thermodynamics. *Fluid Phase Equilib.* **1995**, *104*, 1–20.

(6) Prausnitz, J. M. Thermodynamics of structured fluids. Hard science for soft materials. *Pure Appl. Chem.* **2000**, *72*, 1819–1834.

(7) Prausnitz, J. M. Three frontiers in the thermodynamics of protein solutions. *Pure Appl. Chem.* **2007**, *79*, 1435–1444.

(8) Prausnitz, J. M. Biotechnology: A new frontier for molecular thermodynamics. *Fluid Phase Equilib.* **1989**, *53*, 439–451.

(9) Prausnitz, J. M. Molecular thermodynamics for some applications in biotechnology. *Pure Appl. Chem.* **2003**, *75*, 859–873.

(10) Prausnitz, J. M. Not macro, not micro, but meso: Three coarse-grained methods for thermodynamic properties of partially structured fluids. *Fluid Phase Equilib.* **1998**, *150−151*, 1–17.

(11) Vuks, M. F.; Shurupova, L. V. The scattering of light and phase transition in solutions of tertiary butyl alcohol in water. *Opt. Commun.* **1972**, *5*, 277–278.

(12) Beer, C. W., Jr.; Jolly, D. J. Comments on "the scattering of light and phase transition in solutions of tertiary butyl alcohol in water". *Opt. Commun.* **1974**, *11*, 150–151.

(13) Bender, T. M.; Pecora, R. A dynamic light scattering study of the *tert*-butyl alcohol-water system. *J. Phys. Chem.* **1986**, *90*, 1700–1706.

(14) Kato, S.; Jobe, D.; Rao, N. P.; Ho, C. H.; Verrall, R. E. Ultrasonic relaxation studies of 2-butoxyethanol-water and 2-butoxyethanol-water-cetyltrimethylammonium bromide solutions as a function of composition. *J. Phys. Chem.* **1986**, *90*, 4167–4174.

(15) Euliss, G. W.; Sorensen, C. M. Dynamic light scattering studies of concentration fluctuations in aqueous *t*-butyl alcohol solutions. *J. Chem. Phys.* **1984**, *80*, 4767–4773.

(16) Bender, M. T.; Pecora, R. Dynamic light scattering measurements of mutual diffusion coefficients of water-rich 2-butoxyethanol/water systems. *J. Phys. Chem.* **1988**, *92*, 1675–1677.

(17) Jacob, J.; Anisimov, M. A.; Sengers, J. V.; Oleinikova, A.; Weingärtner, H.; Kumar, A. Novel phase-transition behavior near liquid-liquid critical points of aqueous solutions: Formation of a third phase at the interface. *Phys. Chem. Chem. Phys.* **2001**, *3*, 829–831.

(18) Wagner, M.; Stanga, O.; Schröer, W. Tricriticality in the ternary system 3-methylpyridine/water/NaBr? The light-scattering intensity. *Phys. Chem. Chem. Phys.* **2004**, *6*, 580–589.

(19) Jin, F.; Ye, J.; Hong, L.; Lam, H.; Wu, C. Slow relaxation mode in mixtures of water and organic molecules: Supramolecular structures or nanobubbles? *J. Phys. Chem. B* **2007**, *111*, 2255–2261.

(20) Boström, M.; Tavares, F. W.; Ninham, B. W.; Prausnitz, J. M. Effect of salt identity on the phase diagram for a globular protein in aqueous electrolyte solutions. *J. Phys. Chem. B* **2006**, *110*, 24757–24760.

(21) Debenedetti, P. G. *Metastable Liquids*; Princeton University Press: Princeton, NJ, 1996.

(22) Georgalis, Y.; Kierzek, A. M.; Saenger, W. Cluster formation in aqueous electrolyte solutions observed by dynamic light scattering. *J. Phys. Chem. B* **2000**, *104*, 3405–3406.

(23) Yang, C.; Lei, W.; Wu, C. Laser light-scattering study of solution dynamics of water/cycloether mixtures. *J. Phys. Chem. B* **2004**, *108*, 11866–11870.

(24) Sedlák, M. Large-scale supramolecular structure in solutions of low molar mass compounds and mixtures of liquids: I. Light scattering characterization. *J. Phys. Chem. B* **2006**, *110*, 4329–4338.

(25) Sedlák, M. Large-scale supramolecular structure in solutions of low molar mass compounds and mixtures of liquids: II. Kinetics of the formation and long-time stability. *J. Phys. Chem. B* **2006**, *110*, 4339–4345.

(26) Sedlák, M. Large-scale supramolecular structure in solutions of low molar mass compounds and mixtures of liquids: III. Correlation with molecular properties and interactions. *J. Phys. Chem. B* **2006**, *110*, 13976–13984.

(27) Jin, F.; Ye, X.; Wu, C. Observation of kinetic and structural scalings during slow coalescence of nanobubbles in an aqueous solution. *J. Phys. Chem. B* **2007**, *111*, 13143–13146.

(28) Jacob, J.; Kumar, A.; Anisimov, M. A.; Povodyrev, A. A.; Sengers, J. V. Crossover from Ising to mean-field critical behavior in aqueous electrolyte solution. *Phys. Rev. E* **1998**, *58*, 2188–2200.

(29) Jacob, J.; Anisimov, M. A.; Kumar, A.; Agayan, V. A.; Sengers, J. V. Novel phase-transition behavior in an aqueous electrolyte solution. *Int. J. Thermophys.* **2000**, *21*, 1321–1338.

(30) Jacob, J.; Kumar, A.; Asokan, S.; Sen, D.; Chitra, R.; Mazumdar, S. Evidence of clustering in an aqueous electrolyte solution: A small-angle X-ray scattering study. *Chem. Phys. Lett.* **1999**, *304*, 180–186.

(31) Van Roie, B.; Pitsi, G.; Thoen, J. Calorimetric search for a tricritical point in mixtures of water, 3-methylpyridine and sodium bromide. *J. Chem. Phys.* **2003**, *119*, 8047–8051.

(32) Wagner, M.; Stanga, O.; Schröer, W. Tricriticality in the ternary system 3-methylpyridine/water/NaBr? The coexistence curves. *Phys. Chem. Chem. Phys.* **2003**, *5*, 1225–1234.

(33) Wagner, M.; Stanga, O.; Schröer, W. Tricriticality in the ternary system 3-methylpyridine/water/NaBr? Measurements of the viscosity. *Phys. Chem. Chem. Phys.* **2002**, *4*, 5300–5306.

(34) Schröer, W.; Wagner, M.; Stanga, O. Apparent mean-field criticality of liquid-liquid phase transitions in ionic solutions. *J. Mol. Liq.* **2006**, *127*, 2–9.

(35) Gutkowski, K. I.; Bianchi, H. L.; Japas, M. L. Critical behavior of a ternary ionic system: A controversy. *J. Chem. Phys.* **2003**, *118*, 2808–2814.

(36) Kostko, A. F.; Anisimov, M. A.; Sengers, J. V. Criticality in aqueous solutions of 3-methyl pyridine and sodium bromide. *Phys. Rev. E* **2004**, *70*, 026118.

(37) Anisimov, M. A.; Esipov, V. S.; Zaprudskii, V. M.; Zaugol'nikova, N. S.; Ovodov, G. I.; Ovodova, T. M.; Seifer, A. L. Anomaly in the heat capacity and structural phase transformation of the ordering type in an aqueous solution of *t*-butanol. *J. Struct. Chem.* **1977**, *18*, 663–670.

(38) Anisimov, M. A. *Critical Phenomena in Liquids and Liquid Crystals*; Gordon & Breach Science Publishers: New York, 1991.

(39) Ross, R. G.; Anderson, P. Clathrate and other solid phases in the tetrahydrofuran-water system: thermal conductivity and heat capacity under pressure. *Can. J. Chem.* **1982**, *60*, 881–892.

(40) Mandelcorn, L. Clathrates. *Chem. Rev.* **1959**, *59*, 827–839.

(41) Mak, T. C. W.; McMullan, R. R. Polyhedral clathrate hydrates. X. Structure of the double hydrate of tetrahydrofuran and hydrogen sulfide. *J. Chem. Phys.* **1965**, *42*, 2732–2737.

(42) Glew, D. N.; Mak, H. D.; Rath, N. S. Aqueous non-electrolyte solutions: Part VII Water shell stabilization by interstitial nonelectrolytes. In *Hydrogen bonded solvent system*; Covington, A. K., Jones, P., Eds.; Taylor and Francis: London, 1998; pp 195—210.

(43) Cox, H. L.; Cretcher, L. H. The influence of temperature on the reciprocal solubility of the mono-alkyl ethers of ethylene glycol and water. *J. Am. Chem. Soc.* **1926**, *48*, 451–453.

(44) Novák, J. P.; Matouš, J.; Pick, J. *Liquid-Liquid Equilibria*; Elsevier: New York, 1987.

(45) Jacob, J.; Anisimov, M. A.; Sengers, J. V.; Dechabo, V.; Yudin, I. K.; Gammon, R. W. Light scattering and crossover critical phenomena in polymer solutions. *Appl. Opt.* **2001**, *40*, 4160–4169.

(46) Anisimov, M. A.; Kostko, A. F.; Sengers, J. V. Competition of mesoscales and crossover to tricriticality in polymer solutions. *Phys. Rev. E* **2002**, *65*, 051805.

(47) Kostko, A. F.; Anisimov, M. A.; Sengers, J. V. Dynamic crossover to tricriticality and anomalous slowing down of critical fluctuations by entanglements in polymer solutions. *Phys. Rev. E* **2002**, *66*, 020803(R).

(48) Berne, B. J.; Pecora, R. *Dynamic Light Scattering: With Applications to Chemistry, Biology, and Physics*; Wiley: New York, 1976; Dover Publications: Mineola, NY, 2000.

(49) Fabelinskii, I. *Molecular Scattering of Light*; translated by Beyer, R. T.; Plenum Press: New York, 1968.

(50) Segrè, P. N.; Gammon, R. W.; Sengers, J. V. Light-scattering measurements of nonequilibrium fluctuations in a liquid mixture. *Phys. Rev. E* **1993**, *47*, 1026–1034.

(51) Wang, L. C.; Xu, H. S.; Zhao, J. H.; Song, C. Y.; Wang, F. A. Density and viscosity of (3-picoline + water) binary mixtures from T = (293.15 to 342.15) K. *J. Chem. Thermodyn.* **2005**, *37*, 477–483.

(52) Finney, J. L.; Bowron, D. T.; Soper, A. K. The structure of aqueous solutions of tertiary butanol. *J. Phys.: Condens. Matter* **2000**, *12*, A123–A128.

(53) Iwasaki, K.; Fujiyama, T. Light-scattering study of clathrate hydrate formation in binary mixtures of *tert*-butyl alcohol and water: 2. Temperature effect. *J. Phys. Chem.* **1979**, *83*, 463–468.

(54) Bowron, D. T.; Finney, J. L.; Soper, A. K. Structural investigation of solute-solute interactions in aqueous solutions of tertiary butanol. *J. Phys. Chem. B* **1998**, *102*, 3551–3563.

(55) Mizuno, K.; Kimura, Y.; Morichika, H.; Nishimura, Y.; Shimada, S.; Maeda, S.; Imafuji, S.; Ochi, T. Hydrophobic hydration of *tert*-butyl alcohol probed by NMR and IR. *J. Mol. Liq.* **2000**, *85*, 139–152.

(56) Vásquez, D.; Tora, J.; Lozsán, A.; García-Sucre, M.; Urbina-Villalba, G. Interfacial properties of *tert*-butyl alcohol solutions and their relation to clathrate formation. *J. Phys. Chem. B* **2002**, *106*, 2649–2655.

(57) Fukasawa, T.; Tominaga, Y.; Wakisaka, A. Molecular association in binary mixtures of *tert*-butyl alcohol-water and tetrahydrofuran-heavy water studied by mass spectroscopy of clusters from liquid droplets. *J. Phys. Chem. A* **2004**, *108*, 59–63.

(58) Nishikawa, K.; Iijima, T. Structural study of *tert*-butyl alcohol and water mixtures by X-ray diffraction. *J. Phys. Chem.* **1990**, *94*, 6227–6231.

(59) Harris, K. R.; Newitt, P. J. Diffusion and structure in water-alcohol mixtures: Water + *tert*-butyl alcohol (2-methyl-2-propanol). *J. Phys. Chem. A* **1999**, *103*, 6508–6513.

(60) Bowron, D. T.; Moreno, S. D. The structure of a concentrated aqueous solution of tertiary butanol: Water pockets and resulting perturbations. *J. Chem. Phys.* **2002**, *117*, 3753–3763.

(61) Bowron, D. T.; Moreno, S. D. Structural correlations of water molecules in a concentrated alcohol solution. *J. Phys.: Condens. Matter* **2003**, *15*, S121–S127.

(62) Finney, J. L.; Bowron, D. T.; Daniel, R. M.; Timmins, P. A.; Roberts, M. A. Molecular and mesoscale structures in hydrophobically driven aqueous solutions. *Biophys. Chem.* **2003**, *105*, 391–409.

(63) Paul, S.; Patey, G. N. Why *tert*-butyl alcohol associates in aqueous solution but trimethylamine-*N*-oxide does not. *J. Phys. Chem. B* **2006**, *110*, 10514–10518.

(64) Pradhan, T.; Ghoshal, P.; Biswas, R. Structural transition in alcohol-water binary mixtures: A spectroscopic study. *J. Chem. Sci.* **2008**, *120*, 275–287.

(65) Iwasaki, K.; Fujiyama, T. Light-scattering study of clathrate hydrate formation in binary mixtures of *tert*-butyl alcohol and water. *J. Phys. Chem.* **1977**, *81*, 1908–1912.

(66) Cataliotti, R. S.; Palombo, F.; Paolantoni, M.; Sassi, P.; Raudino, A. Concentration fluctuations and collective properties in mixed liquid systems: Rayleigh-Brillouin spectra of *tert*-butyl alcohol/2,2′-dimethylbutane liquid mixture. *J. Chem. Phys.* **2007**, *126*, 044505.

(67) Nishikawa, K.; Hayashi, H.; Iijama, T. Temperature dependence of the concentration fluctuation, the Kirkwood-Buff parameters, and the correlation length of *tert*-butyl alcohol and water mixtures studied by small-angle X-ray scattering. *J. Phys. Chem.* **1989**, *93*, 6559–6565.

(68) Jacobson, L. C.; Hujo, W.; Molinero, V. Amorphous precursors in the nucleation of clathrate hydrates. *J. Am. Chem. Soc.* **2010**, *132*, 11806–11811.

(69) Sloan, E. D.; Koh, C. A. *Clathrate Hydrates of Natural Gases*; Taylor and Francis: Boca Raton, FL, 2008.

(70) Sprindler, L.; Olenik, I. D.; Čopič, M.; Mariani, P. The effect of temperature on the self-assembly of deoxyguanosine 5-monophosphate in pretransitional region of the i-ch phase transition. *Mol. Cryst. Liq. Cryst.* **2004**, *409*, 43–50.

(71) Serwicka, K.; Marczak, W. Association in dilute aqueous solution of pyridine and its methyl derivatives studied by cryoscopic method. *Int. J. Thermophys.* **2011**, DOI: 10.1007/s10765-010-0792-y.

(72) Kasraian, K.; DeLuca, P. P. Thermal analysis of the tertiary butyl alcohol-water system and its implications on freeze-drying. *Pharm. Res.* **1995**, *12*, 484–490.

(73) Sadakane, K.; Onuki, A.; Nishida, K.; Koizumi, S.; Seto, H. Multilamellar structures induced by hydrophilic and hydrophobic ions added to a binary mixture of D_2O and 3-methylpyridine. *Phys. Rev. Lett.* **2009**, *103*, 167803.