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Laboratory Experiment

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Learning about Structural and Optical Properties of Organic Compounds through Preparation of Functional Nanomicelles while Avoiding Hazardous Chemicals or Complicated Apparatus

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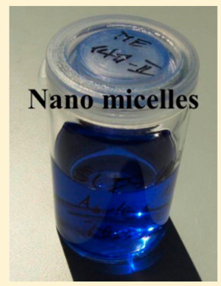
Supporting Information

ABSTRACT: The synthesis of nanomicelles in the aqueous phase on the basis of nonhazardous detergents is described where azulene and a naphthalene tetracarboximide are used in this experiment to teach the relation between structural and optical properties of organic compounds and point out possible applications. The experiment covers many aspects of modern-day chemistry; a simple handling of nonhazardous reagents makes the system suitable for basic chemical education even for comparably moderately skilled persons.



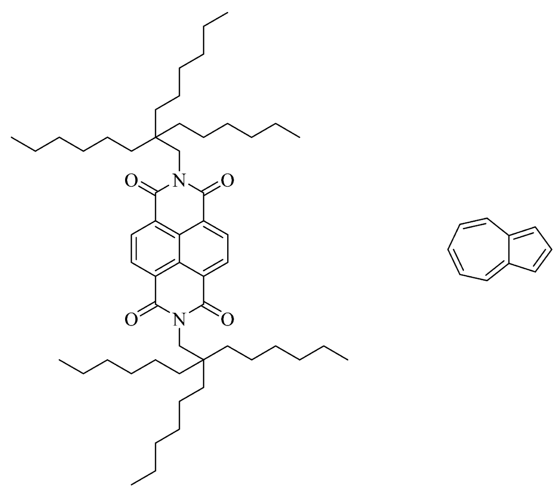
KEYWORDS: *Nanotechnology, Micelles, Undergraduate Research, Aromatic Compounds*

■ INTRODUCTION

Nanotechnology is becoming more and more attractive in research and technology. As a consequence, experiments with nanomaterials[1] are of special interest both for academic and school education. However, the common generation of nanomaterials often requires special equipment and hazardous chemicals; the risks of nanomaterials are being presently discussed.[2] The application of functional nanomaterials in the aqueous phase is a convenient way for nonhazardous chemistry. The generation of micelles and microemulsions and their intrinsic properties, such as the structure or the critical micelle concentration (CMC) were the focus of well-established research.[3] However, few such systems have been discussed as functional nanoparticles. We dispersed lipophilic fluorescent dyes in the aqueous phase to obtain highly fluorescent nanodispersions, and discussed these findings in previous publications.[4] Connecting the fluorescent chromophore with amino groups as efficient electron donors for light driven charge-transfer causes fluorescence quenching by electron transfer. Protonation of the amino groups blocks the electron transfer, effectively turning such a system into a nano pH indicator.[5]

We started further research with the concept of nanomicelles focusing on colorful azulene and the naphthalene-1,4:5,8-tetracarboxylic bisimide **1**, which both exhibit interesting optical and functional properties (Figure 1).

We aimed to create an experiment for undergraduate students that incorporates interesting aspects of modern-day chemistry, avoids hazardous materials, and is easy to carry out even for minimally skilled persons. The chamomile-derived azulene and its derivatives are known to exhibit anti-inflammatory properties and therefore are applied in skin-care products.[6,7] Additionally, azulene exhibits an easily visible brilliant blue color in lipophilic media and is considered nonhazardous. Naphthalene as its isomer, on the other hand, absorbs only in the UV-region, a fact that has been discussed in the past.[8] We used the naphthalene-1,4:5,8-tetracarboxylic bisimide **1**; this class of naphthalene derivative is reported as intense UV-A light absorber[9] and is currently studied as a potential sun-blocking agent in cosmetics due to its absorption properties.[10]



1 **2**

Figure 1. Naphthalene-1,4:5,8-tetracarboxylic bisimide (**1**, MW, 827.29 g/mol) and azulene (**2**, CAS, RN 275-51-4; MW, 128.17 g/mol).

To create the micelles, we decided to use cocamidopropyl betaine (CAPB) **3** and sodium laureth sulfate (SLES) **4** (Figure 2), which are known to be much less aggressive to the human skin compared to other detergents often used in experiments such as sodium dodecyl sulfate (SDS).[11−13]

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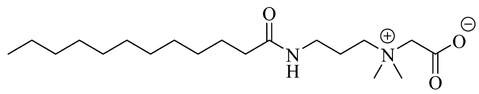

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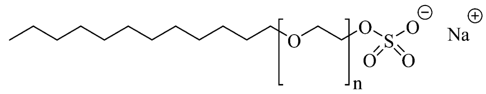

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Figure 2. Detergents cocamidopropyl betaine (**3**; CAS, RN 86438-79-1; MW, 342.52 g/mol), sodium laureth sulfate (**4**; sodiumdodecylpoly-(oxyethylene)sulfate; CAS, RN 9004-82-4; n = 3: SLE3S MW, 309.44 g/mol).

Both detergents are used in many skin-care products, are well-tested, and have international approval for skin applications.[14,15] The Critical Micelle Concentration (CMC) for pure detergents is 0.06% for sodium laureth sulfate with $n = 3$ and 0.063% for cocamidopropyl betaine.[16]

Finally, the characterization of the nanostructure generally requires sophisticated equipment not available in basic chemical education. As an alternative, we found that simple blue ribbon paper filter as standard equipment in chemical labs is able to separate nano- from microparticles.[17] Thus, we could develop a very simple and straightforward setup for the generation and identification of nanoparticles.

■ EXPERIMENTAL METHODS

The particular compound was treated with an aqueous solution of the respective detergent (30% (**3**)/28% (**4**)), stirred at 50 °C for 10 min, diluted with distilled water, stirred at 50 °C for another 20 min (complete dissolution of the compound), and filtered through a blue ribbon paper filter (Sartorius Stedim Quantitative Papers FT-3-104-055, blue dot, grade 391) for removal of traces of residual microparticles and indication of the nanodimensions of the components. A perfectly clear phase passed the filter, with almost no material held back by the filter. The nanomicelles in aqueous solution were stable for over a year. The nanodimensions of the micelles could be confirmed by dynamic light scattering. The device used for determination of the size of the nanomicelles was a *Malvern Nano ZS* with a detection range of 0.6 nm to 6 μm. It uses a 4 mW He-Ne-Laser with a wavelength of 633 nm and an avalanche photodiode for detection. The device was calibrated using polymer microspheres in water (Nanosphere Size Standards No. 3060A, NIST traceable mean diameter 60 ± 2.5 nm). The samples were prepared as-is in semi-micro disposable PMMA cuvettes (BRAND standard disposable cuvettes) and needed no further dilution. The data for each sample was collected in 10 runs (10 s each) at room temperature using the backscatter method. The data was obtained as intensity (%) and is displayed as intensity (%) in cumulative plots.

■ RESULTS

The maxima of the distribution of the micelles containing compound **1** were about 4 nm for cocamidopropyl betaine (**3**) and even smaller at slightly more than 1 nm for sodium laureth sulfate (**4**). There are no larger particles, and this explains that no light scattering could be visually observed. For comparison, measurements were also performed with the micelle-containing solutions before filtration, but no particles could be found within the detection range of the DLS-device (0.6 nm to 6 μm) (Figure 3). Actually, those solutions were quite murky, and larger particles could be observed with the naked eye.

The UV/vis-spectrum of **1** in nanomicelles of **3** is reported in Figure 4. It is similar to the spectrum of **1** in lipophilic ethyl acetate, which was chosen as solvent because of its low toxicity compared to other lipophilic solvents and may be easily reproduced with this solvent.

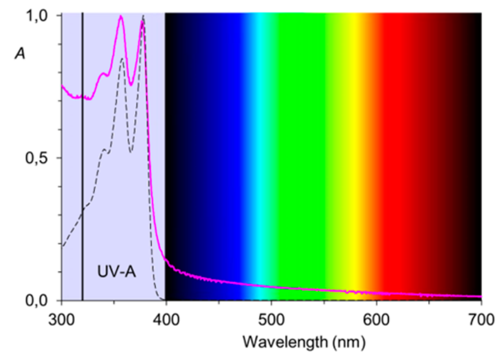

Figure 4. UV/vis spectra of **1** in nanomicelles of **3** (solid line) compared with the spectrum in ethyl acetate (dashed line) and indicated UV-A region. Abscissa: Wavelength in nm. Ordinate: Normalized Absorption.

This indicates that the dye molecules of **1** are in lipophilic microenvironment in the micelles, since the dye itself is insoluble in aqueous media. The UV-A region is fully covered, whereas the visible region remains transparent; the gently inclined baseline to longer wavelengths is a consequence to slight light-scattering by the micelles. These solutions have great potential to be used for

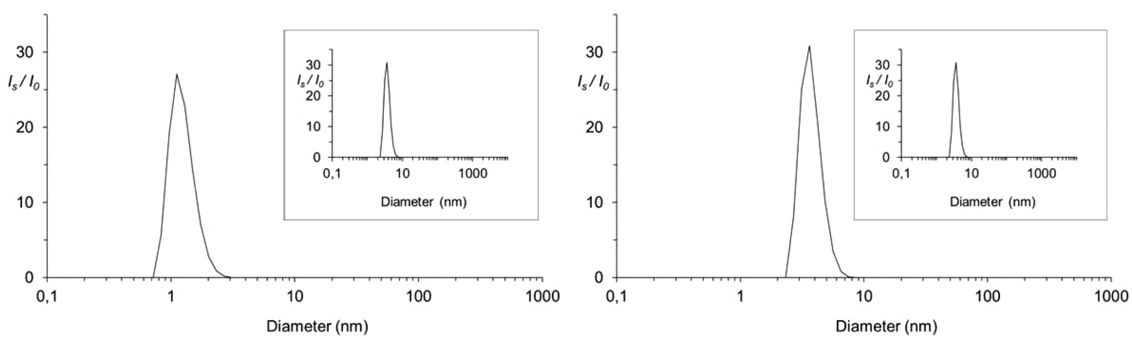

Figure 3. Dynamic light scattering (DLS) measurements of the naphthalene derivative **1**-containing micelles of sodium laureth sulfate (**4**) (left) and cocamidopropyl betaine (**3**) (right) in water. Insert: Expanded abscissa.

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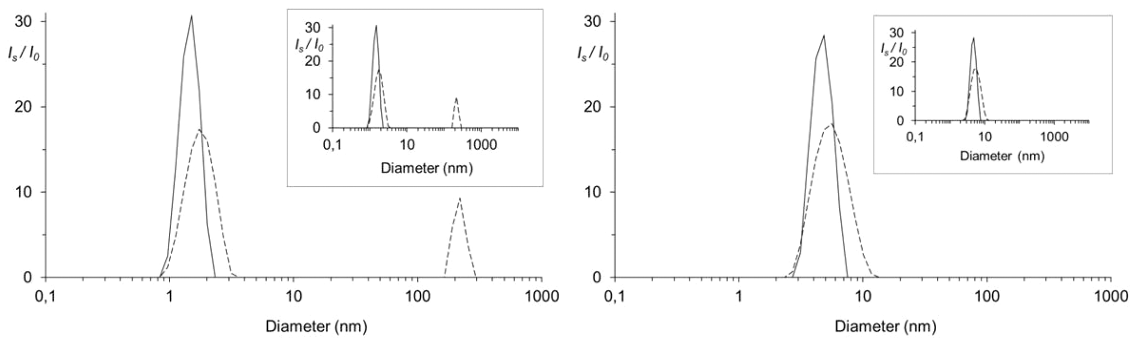

Figure 5. Dynamic light scattering (DLS) measurements of azulene-containing micelles of sodium laureth sulfate (**4**) (left) and cocamidopropyl betaine (**3**) (right) in water. The data of the filtered solution (solid line) is compared with that of the respective solution before filtration (dashed line). Insert: Expanded abscissa.

sun protection in skin-care products, because a colorless material fully absorbs in the UV.

The successful demonstration of the simple generation of functional nanomicelles can be transferred to azulene (**2**) as well. Micelles of azulene in water were obtained the same way as described for **1** and gave similar distributions in size in a perfectly clear, intensely blue liquid. An average of about 6 nm was obtained for azulene-containing micelles of cocamidopropyl betaine; micelles of sodium laureth sulfate were even smaller at slightly more than 1 nm, as shown in Figure 5. This was confirmed by the simple blue ribbon filtration where only nanoparticles are able to pass.

Comparison with the data of the solutions before filtration shows that larger particles are held back by the filter paper for micelles of sodium laureth sulfate. For micelles of cocamidopropyl betaine, no larger particles are observed within the detection range of the DLS-device.

The intensely blue color of the azulene-containing nanomicelles in water corresponds to the same color of azulene in lipophilic media such as ethyl acetate and corresponds to the UV/vis-spectra shown in Figure 6. The similarity of the spectra

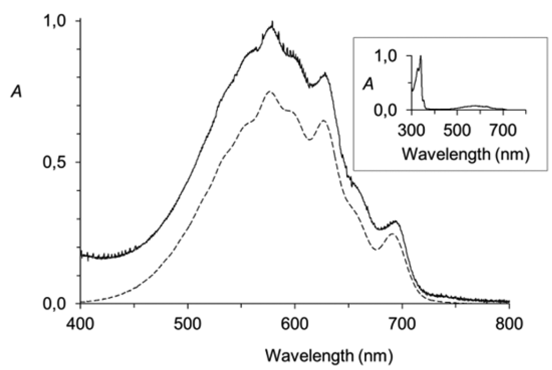

Figure 6. UV/vis spectrum of azulene in nanomicelles in water (solid line) compared with azulene dissolved in ethyl acetate (dashed line, normalized to 0.75 for better clearness). Insert: Compressed spectrum of azulene in nanomicelles.

indicates that azulene resides in the lipophilic microenvironment in the interior of the micelles, since azulene itself is insoluble in water.

■ HAZARDS

One objective of this experiment was to avoid the use of hazardous materials. Azulene (**2**) is considered nonhazardous, exhibits anti-inflammatory properties and thus is used in skin-care products. It has regulatory approval in many countries. The naphthalene-1,4:5,8-tetracarboxylic bisimide (**1**) is currently studied as potential sun-blocking agent in cosmetics and is estimated to be nonhazardous; however, since this is still an ongoing development, there are no regulatory approval for applications and therefore the use of safety eyewear, nitrile gloves, and lab coats is recommended.[10] The detergents used within this experiment have got regulatory approval for their application in cosmetics in many countries and are widely used in skin-care products.[14,15] For the use of cocamidopropyl betaine (CAPB), there have been concerns regarding its potential as an allergen, resulting in it being voted “Allergen of the year” by the American Contact Dermatitis Society in 2004.[18] However, a double-blind randomized controlled pilot study suggests that “doubtful and mild reactions to CAPB may represent irritant reactions as opposed to true allergic reactions”, whereas other studies found that most apparent allergic reactions are more likely caused by amidoamine, “which is a known contaminant of technical CAPB preparations”.[19,20] Thus, “when thoroughly purified, it no longer has a sensitizing action”.[21]

■ DISCUSSION

This experiment has been successfully tested with 76 undergraduate (Bachelor) students in groups of six persons during a practical course, which aimed to teach important aspects of recent chemistry while avoiding hazardous materials. This course is part of basic education in organic chemistry at the Ludwig-Maximilians University in Munich. Aspects of the experiment that were discussed with the students included the relation between structural and absorption properties using azulene and naphthalene as examples, as well as the application of DLS and UV/vis spectroscopy as analytical methods. The students were taught the basic principles of micelle formation, different classes of detergents and possible applications of the nanomicelles they created. Even comparably low skilled persons could follow the operation procedure without problems. The students had to produce a record of the experimental procedure and their results after the course, which was graded by the instructors.

The experiment was established with the dyes and detergents described above. Various dyes and detergents may be used by the students. However, other dyes might be more difficult to solubilize and different detergents might exhibit minor efficiencies. For example, carboxylate salts such as sodium myristate or caprylate did not prove as suitable detergents for obtaining the targeted nanomicelles; the particular chemicals

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have to be individually tested. Other commonly used detergents such as sodium dodecyl sulfate (SDS) also work; however, they might act as skin irritants and thus are not attractive for experiments that aim to avoid hazardous materials. For more information please see the Supporting Information. Instead of stirring the compounds, an ultrasonic bath can be applied as well, but stirring has proven to yield better results, i.e., smaller micelles and no aggregates, and is more simple and convenient. Depending on how many different dyes and detergents are used, the students may carry out the experiment within 1–2 days.

■ CONCLUSION

Concluding, nanotechnology can be demonstrated without the application of hazardous components or sophisticated apparatus in basic chemical education. Nanomicelles can be prepared from materials with low molecular weights such as azulene as guests in well-tested, nonhazardous detergents as hosts in the aqueous phase. Color effects and filtration through paper filters with very low pore sizes obviously indicate the solubilization in water and the nanosize of the particles.

The nanomicelles containing the naphthalene-1,4:5,8-tetracarboxylic bisimide (**1**) might be used as a sun-blocking agent in future applications. Common sunscreen cosmetics often use titanium dioxide or zinc oxide nanoparticles for the absorption of UV light. However, recent research indicates that such particles may pose a health risk, as it has been shown that ZnO nanoparticles for instance can induce DNA damage and cytotoxicity and therefore require further treatment, e.g., coating.[22] One may demand alternative materials which absorb in the UV region and do not affect the human body. The azulene nanomicelles might be suitable for application as after-sun treatment, as azulene has anti-inflammatory properties and is already used in skin-care products.

■ ASSOCIATED CONTENT

Supporting Information

Required chemicals; required laboratory equipment; safety and hazards; general procedure; learning objectives; references. This material is available via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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