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Task-Specific, Biodegradable Amino Acid Ionic Liquid Surfactants

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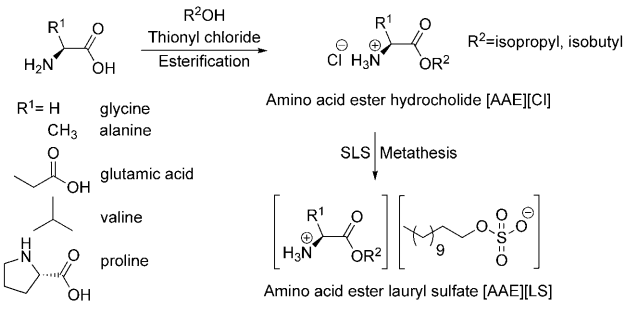
Besides several conventional uses, such as in cleaning products, food, beverages, dairy processing, water treatment, healthcare, fuel and lubricant additives, and emulsifiers or stabilizers in paints or cosmetics, there is an increasing interest in the synthesis of new surfactants for high-end applications such as gene transfection agents, the denaturation/encapsulation of proteins or drugs, or templates for shape- or size-selective and highly ordered nanomaterials.[1] Because of their modular nature and unique physicochemical properties, ionic liquids (ILs) have found widespread application and are used in many areas of chemistry.[2] The inherent amphiphilic character of some ILs has yielded surface-active properties that are different (and better) than those of conventional surfactants, and thus they have emerged as a superior class of surfactants.[3] Also, conventional ionic surfactants suffer from phase separation, owing to solubility limitations, and the fact that the creation of hierarchical micellar systems is usually thermodynamically unfavorable. This restricts their use in many applications, for example, as templates for a desired nanomaterial architectures.[4] In contrast, owing to their strong and directional polarizability and excellent water solubility ILs have been shown to self-assemble into highly structured forms, useful for the preparation of a variety of nanomaterials (e.g., metals, metal oxides, zeolites).[5]

Although IL surfactants used so far are "green" in terms of their negligible vapor pressure, they generally contain synthetic quaternary nitrogen cations (such as alkylammonium, dialkylimidazolium, or pyridinium) with halogen atoms as anions (such as Cl or F). They can release HCl or HF by hydrolysis under certain conditions, which may pose a hazard when they are released into the environment through wastewater effluents. Therefore, toxicity and biodegradation are vital issues when dealing with ILs.[6]

In this context, the green credentials of ILs have been tremendously improved by the development of biobased ILs.[7] Herein, we choose natural amino acids and sodium lauryl sulphate (SLS) as precursors for amino acid ionic liquid surfactant (AAILS) architectures. Amino acid-based surfactants, featuring amino acids modified with long aliphatic chains to generate linear, dimeric, or glycerolipid-like structures, have been reported extensively,[8] however, ionic liquid surfactants based on amino acids having a superior surface activity and solvent miscibility are reported here for the first time. From the natural amino acids, L-glycine, L-alanine, L-valine, L-glutamic acid, and L-proline were chosen allow simple variations in the side chain through branching, the addition of another –COOH group, or cyclization. Because the incorporation of an ester group into an amino acid has been shown decrease the melting point and significantly increase biodegradability,[9] esterification of the amino acids was carried out by using either isopropyl or isobutyl alcohol.

For esterification, thionyl chloride was slowly added to isopropyl or isobutyl alcohol at 0 °C. Amino acids were slowly added to the reaction mixtures, which were then refluxed for 4 h. The reaction mixtures were concentrated in a rotary evaporator, and crude amino acid ester hydrochlorides were titurated with hexane at 0 °C. Pure crystals of amino acid ester hydrochlorides (AAECls) were obtained by recrystallization with methanol/hexane. Equimolar amounts of the AAECls and SLS were then dissolved in hot water. After the completion of reaction, water was removed under vacuum and AAILSs were extracted by the addition of dichloromethane. All of the AAILSs except the one obtained from glutamic butyl ester hydrochloride (white crystalline solid at room temperature) were clear but slightly viscous liquids at room temperature. The reaction sequence is shown in Scheme 1. Detailed preparation, washing, and drying procedures can be found in the Supporting Information. The structures of the AAILSs were confirmed by



Scheme 1. Synthesis of AAILSs.

NMR (^{1}H and ^{13}C), elemental analysis (CHNS), and electrospray ionization mass spectrometry (ESI-MS). Herein, we use general symbols to represent the amino acids, and use the number of carbon atoms to represent the alkyl groups of the ester (e.g., glycine propyl ester lauryl sulphate is denoted as $Gly C_3 LS$).

Physicochemical properties of the AAILSs are listed in Table 1. Differential scanning calorimetry (DSC) analysis re-

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Table 1. Physicochemical properties of synthesized AAILSs.

Sample	T_m [°C]	T_g [°C]	T_d [°C]	$[\alpha]_D^{30}$[a]	ρ[b] [g cm^{-3}]	κ[b] [mS cm^{-1}]	cac[b] [mM]	γ_{cac}[b] [mN m^{-1}]
$GlyC_3LS$	5	−18	243	–	1.0503	0.01015	0.63	26.0
$GlyC_4LS$	35	−5	257	–	1.0174	2.415	0.43	27.0
$AlaC_3LS$	−3	−34	244	+0.77	1.0469	0.08848	0.53	25.7
$AlaC_4LS$	−12	−33	268	−1.03	1.0418	3.95	0.49	28.5
$GluC_3LS$	30	−43	221	+9.57	1.0503	1.082	0.67	30.6
$GluC_4LS$	56	−19	230	+8.83	1.0331	–	–	–
$ValC_3LS$	26	−19	272	+6.71	1.0261	0.01308	0.68	27.5
$ValC_4LS$	26	−27	279	+5.86	1.0093	1.814	0.28	30.6
$ProC_3LS$	−15	−33	247	−14.58	1.0468	0.059	0.48	27.8
$ProC_4LS$	−22	−46	280	−18.60	1.0359	1.023	0.42	30.5

[a] Concentration: 2 g per 100 mL MeOH. [b] At 25 °C.

vealed a melting temperature (T_m) < 30 °C for all AAILSs except $GluC_4LS$ (T_m = 56 °C). T_m varies with the structure of amino acids, being lowest for $ProC_3LS$ and highest for $GluC_4LS$. The glass transition temperature (T_g) also varied with the structure of amino acids, and was normally < 0 °C. All AAILSs were significantly thermally stable as can be seen from their decomposition temperature (T_d) values of > 220 °C, obtained from thermogravimetric analysis (TGA, Table S1). DSC and TGA profiles of all AAILSs are provided in Figures S1 and S2. Since amino acids and their ester hydrochloride salts have chiral centers that are retained in the final products, we measured the specific rotations ($[\alpha]_D^{30}$) of the synthesized AAILSs (Table 1). These were found to be only slightly less than those of the corresponding amino acid precursors, implying their use as stereoselective catalytic media for organic reactions. Table 1 also shows density and conductivity data. The density of the AAILSs does not vary much with structural changes in amino acids while there is a large variation in conductivity values. AAILSs that have propyl group are slightly more dense and much less conductive than their butyl analogues. A monotonic increase of the conductivity was observed with the increase in temperature.

The conductivity data can be reasonably well fitted to the Vogel–Fulcher–Tammann (VFT) equation.[10] The fitted curves and experimental data are shown in Figure 1. The best-fit parameters for specific conductivity are given in Table S1. Consistent with the literature,[11] the VFT temperatures are below the T_g.

The critical aggregation concentration (*cac*) and surface tension at *cac* (γ_{cac}) values of AAILSs are lower than analogous conventional ionic surfactants by an order of magnitude.[12] Table 2 compares the *cac*'s of the AAILSs to conventional surfactants or ionic liquids with the same alkyl chain length.[13] Figure 2 shows the tensiometry profile of a representative AAILS ($ProC_3LS$). Transmission electron microscopy (TEM) and a dynamic light scattering (DLS) plot (Figure 2, inset) revealed stable spherical aggregates of ca. 4 nm in size.

The biodegradability of the synthesized AAILSs was checked by periodic surface tension measurements of solutions of AAILSs in natural sea water (50 mg L^{-1}). The increase in surface tension with time (Figure 3a) gave a qualitative measure of AAILSs biodegradation by marine bacteria (the status of the marine bacteria in sterilized and natural sea water, with or without addition of AlaC3LS is shown in Figure 3b. The surface tension of all the AAILSs solutions reached the value of natural sea water within 36 h, indicating rapid and complete biodegradability.

Biosurfactants such as glycolipids and lipoproteins, produced from natural compounds by various groups of microorganisms, have been shown to be potential agents for managing harmful algal blooms (HABs), which have severe adverse effects on fisheries, aquacultures, drinking water, tourism, and human health.[14] However, these biosurfactants suffer from high production and recovery costs, while mass production is also difficult. AAILSs, being highly biodegradable and surface active, may mimic the effects of biosurfactants as anti-HAB agents while retaining the advantage of ecological acceptability.

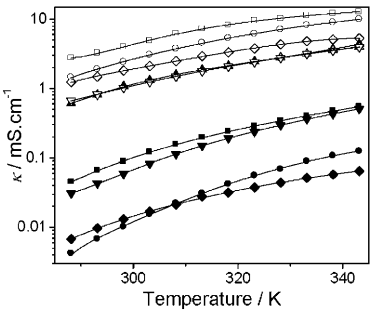

Figure 1. Temperature dependence of ionic conductivity in AAILSs: (■) $AlaC_3LS$, (●) $GlyC_3LS$, (▲) $GluC_3LS$, (▼) $ProC_3LS$ (◆) $ValC_3LS$. Hollow symbols correspond to butyl analogues of AAILSs. VFT data is plotted as solid lines.

Table 2. Comparison of *cac*'s of the synthesized AAILSs to amphiphilic ionic liquids or conventional surfactants with similar alkyl chain lengths (at 25 °C).

AAILSs	*cac* [mM]	Ionic liquid/conventional surfactant	*cac* [mM]	Ref.
$AlaC_3LS$	0.63	1-dodecyl-3-methylimidazolium chloride	13.47	[13a]
$GlyC_3LS$	0.43	1-dodecyl-3-methylimidazolium bromide	10	[13b]
$GluC_3LS$	0.53	1-dodecyl-3-methylpyridinium chloride	13	[13b]
$ProC_3LS$	0.49	1-dodecyl-3-methylpyridinium bromide	10	[13b]
$ValC_3LS$	0.67	1-dodecyl-1-methylpiperidinium bromide	11	[13b]
$AlaC_4LS$[a]	–	1-dodecyl-1-methylpyrrolidinium bromide	13.5	[13c]
$GlyC_4LS$	0.68	sodium dodecyl sulfate	8.0	[13d]
$GluC_4LS$	0.28	dodecyl trimethyl ammonium chloride	21.5	[13d]
$ProC_4LS$	0.48	–	–	
$ValC_4LS$	0.42	–	–	

[a] The *cac* of $AlaC_4LS$ could not be detected due to solubility limitations.

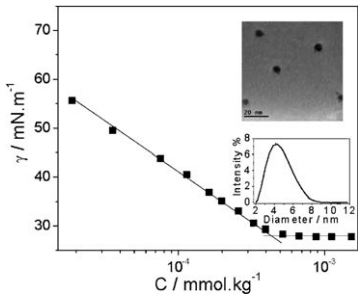

Figure 2. Surface tension of aqueous solutions of a representative AAILS ($ProC_3LS$). The breaking point indicates the *cac*. Insets: TEM and DLS data, indicating an aggregate size in the range of 4–5 nm.

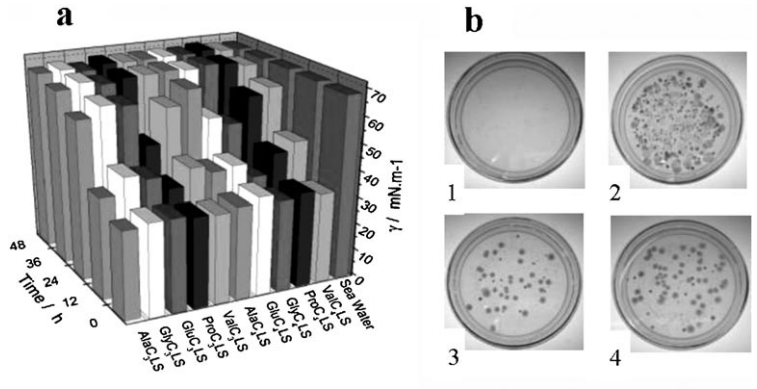

Figure 3. (a) Time-dependent surface tension measurements of solutions of the AAILSs in natural sea water (50 mg L^{-1}). (b) Bacterial colony forming units in (1) sterilized sea water, (2) natural sea water diluted by a factor of 100, (3) an $AlaC_3LS$-sea water solution after 12 h, and (4) an $AlaC_3LS$-sea water solution after 36 h. The volumes of inoculums was 100 μL.

Another potential application of AAILSs was explored: the generation of shape- and size-specific nanostructured materials of technological importance. CeO_2, which is applied in amongst others automotive three-way catalysis, solid oxide fuel cells, metal-oxide semiconductor devices, and gas sensors was chosen as test material. Imidazolium-based ionic liquids with long alkyl chain lengths have been used as both template and solvent for the synthesis of spherical aggregates of CeO_2 nanocrystals or mesostructured crystalline CeO_2.[15] However, the use of AAILSs as structure-directing agents can be advantageous because of not only their green nature, but also because they may allow distinct morphological control owing to the structural and physical properties of amino acids, such as their ability to coordinate to metal ions, the type and length of the functional groups, or their influence on intrinsic electric fields.[16] The synthesis of nearly monodisperse CeO_2 structures was carried out by using a cerium ammonium carbonate solution precursor in the presence of $AlaC_3LS$ under reflux or hydrothermal conditions (see Supporting Information). Reflux conditions produced monodisperse nanospheres, whereas hydrothermal conditions generated monodisperse cubes and star-shaped structures just by varying the precursor concentration (see SEM images in Figure 5a–c).

All samples comprised nanocrystalites 5–14 nm in size (Figure 5d and e). X-ray diffraction (XRD) of synthesized samples calcined at 400 °C revealed well-resolved diffraction peaks which can be indexed to the (111), (200), (220), (311), (222), (400), and (331) planes of a cubic fluorite structured CeO_2 (JCPDS 34-0394) (Figure 5f). Other interesting and useful morphologies can be generated by varying parameters such as temperature, reaction time, or type of AAILS.

In conclusion, we have synthesized novel highly biodegradable amino acid-based ionic liquid surfactants with better surface activity than conventional surfactants, and have demonstrated their potential application in areas such as the mitigation of harmful algal blooms from sea water and the of shape- and size-specific synthesis nanomaterials. Their high solubility

Therefore, the application of representative AAILSs ($AlaC_3LS$ and $AlaC_4LS$) towards the mitigation of HABs comprising *Amphidinium cartarae*, a toxic phytoplankton (Dinoflagellate) was studied. Treatments with 50 μM of $AlaC_3LS$ and $AlaC_4LS$ to inoculums of culture containing 1500 ± 50 cells led to 100% mortality in 24 and 72 h, respectively, indicating that AAILSs with a propyl ester functionality are more effective than butyl analogues (Figure 4a). Lower concentrations, however, had little effect on cell viability in the stipulated experimental time periods. The presence and numbers of dead cells were determined by Evan's Blue staining. The cells were incubated for 10 min and then counted in an inverted microscope in bright mode (Figure 4b shows the impact of AAILS on the test organism; details concerning isolation of the test organism and experimental methodology are provided in the Supporting Information). Results show that very low concentrations of AAILSs are sufficient to provoke an algicidal effect while avoiding detrimental environmental effects. The very high biodegradability of AAILSs ensures ensure their quick disappearance from a marine environment after HAB mitigation.

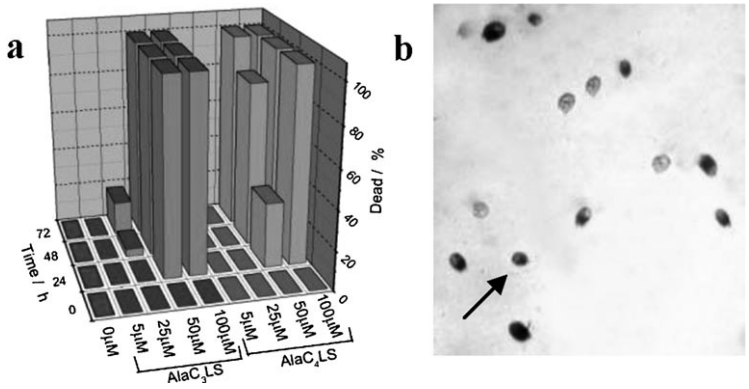

Figure 4. (a) Mortality (%) of Amphidinium cartarae as function of AAILS concentration and time. (b) Impact of 50 μM $AlaC_4LS$ after 24 h (a dead cell is indicated by the arrow; Evan's Blue staining is indicative of dead cells).

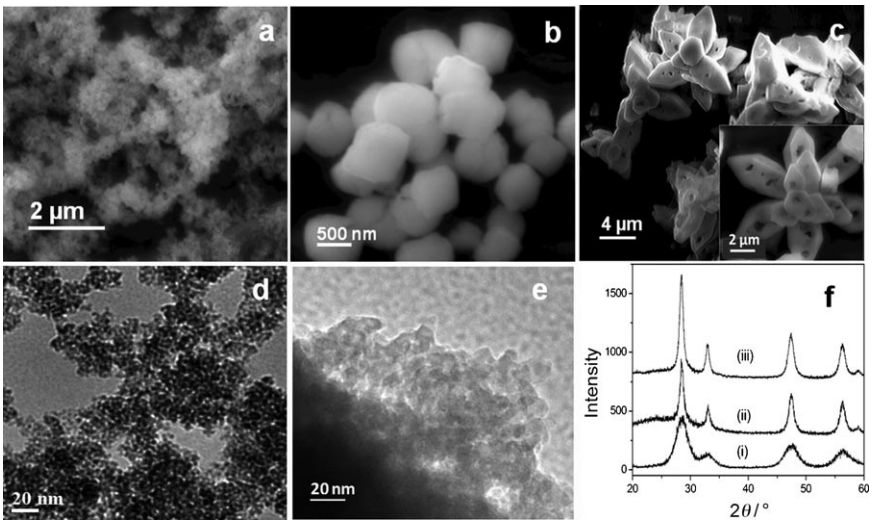

Figure 5. SEM images of CeO_2 nanoparticles: (a) spheres, (b) cubes, (c) stars. Panels (d) and (e) show TEM images corresponding to panels (a) and (b), respectively. (f) XRD patterns of all three structures: (i) spheres, (ii) cubes, (iii) stars.

in water, biodegradability, and nontoxic nature features that make them attractive for biological and drug-delivery applications. In addition, these kinds of surfactants have the ability to bind metallic nanoparticles, based on which biomolecular devices may be fabricated.

Experimental Section

All reagents and solvents were analytical-grade materials purchased from commercial sources, and were used without further purification unless stated otherwise. NMR spectra were recorded in [D_6]DMSO on a Bruker 200 MHz instrument with tetramethyl silane (TMS) as an internal standard. FTIR spectra were recorded by using a Spectrum GX Series 49387 instrument. Elemental analyses were performed on Perkin elmer series II-2400-CHNS. Electrospray ionization mass spectrometry (ESI-MS) was done with a Q-Tof micro Micromass (UK) instrument. Details for all the experimental investigations are given in the Supporting Information. All samples for the measurements of physicochemical properties were dried by heating at 70 °C for at least 7 h under high vacuum. The moisture content, determined by Karl-Fischer titrations„ was less than 0.04 mass %.

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Keywords: amino acids · ionic liquids · nanostructures · surfactants · template synthesis

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