Self-assembled single-chain oligo(*p*-phenylene) amphiphiles: reversed micelles, vesicles and gels

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The diverse supramolecular chemistry of a rigid, T-shaped single-chain amphiphile, including giant vesicles, spherical and tubular reversed micelles, and gels, is described in comparison to that of rigid-rod amphiphiles of different length.

Classical surfactants are single-chain amphiphiles that consist of a flexible lipophilic chain attached to a hydrophilic head group.[1–5] To better organize their dynamic micellar or vesicular suprastructures, design and synthesis of single-chain amphiphiles with either very short (< 11 Å)[2,4] or very long (rod-coil polymers)[6] rigid-rod subunits have been the subject of recent pioneering reports. Despite the potential importance for modern-day nanotechnology and biophysics, comparable studies with oligomeric rigid-rod single-chain amphiphiles are rare, presumably because of the formidable synthetic challenges involved.[7–9] We have recently considered self-assembly of oligo(*p*-phenylene) amphiphiles (*e.g.* **1**–**4**, Fig. 1) as a possible explanation for the poor binding of rigid-rod guests with either asymmetric (*e.g.* **1**) or hydrophobically mismatched (*e.g.* **3**, **4**) scaffolds to lipid bilayer hosts.[8–11] Here we report self-assembly of 'rigid-T' single-chain amphiphile **1** into giant vesicles ($\mathbf{1_v}$), reversed micelles ($\mathbf{1_m}$), and aqueous gels ($\mathbf{1_g}$) in comparison to amphiphilic oligo(*p*-phenylene) rods of different length (**2**–**4**) that yield vesicles only.

'Rigid-rod' vesicles $\mathbf{1_v}$–$\mathbf{3_v}$ were prepared with entrapped HPTS (8-hydroxypyrene-1,3,6-trisulfonic acid, a water soluble fluorescence probe). To obtain vesicles, fully hydrated mixed micellar solutions containing **1**–**4** (2 mM), octyl D-glucopyranoside (70 mM), HPTS (100 μM), and buffer (5–10 mM $Na_nH_{3-n}PO_4$, 0–100 mM NaCl, pH 6.4) were dialysed at 60–70 °C to remove detergent and external HPTS.[9–11] On the other hand, reversed micelles $\mathbf{1_m}$ were made from a solution of 'rigid-T' amphiphile **1** in biphasic systems composed of a nonpolar solvent (*e.g.* $CHCl_3$, CH_2Cl_2, xylene) and either acidic (pH 1, $\mathbf{1_{m(a)}}$) or basic (pH 13, $\mathbf{1_{m(b)}}$) water with HPTS. After brief sonication, rhythmical shaking (1 h, 1300 rpm), and centrifugation (10 min, < 3000*g*), most of the aqueous layer was a milky, foamlike emulsion. This emulsion was stable for more than two weeks but transformed into a gel ($\mathbf{1_g}$, gel point: 1.0 mg ml^{-1})[12] within 3–5 h after removal of the organic phase containing micellar $\mathbf{1_m}$.

The spectroscopic changes of rigid-rod chromophores **1**–**4** upon self-assembly, namely hypo-/hypsochromism of the ^1L transitions and bathochromic shifts for emission maxima, are listed in Table 1. The effects reached from minor changes for 'rigid T's' ($\mathbf{1_v}$/$\mathbf{1_m}$) to unambiguous H-aggregation[13] for rigid rods $\mathbf{2_v}$ and $\mathbf{3_v}$. This implied herringbone-type packing for self-assembled rods of 30 to 40 Å length with multiple constructive π–π-interactions at least for the latter case. An increased tendency toward herringbones for longer rods may further account for crystallization ($\mathbf{4_c}$) instead of vesiculation of deci(*p*-phenylene) **4** under identical conditions.

Consistent with the spectroscopic trends, differential scanning calorimetry (DSC) gave phase transitions for $\mathbf{1_v}$ but not for $\mathbf{2_v}$, $\mathbf{3_v}$ and $\mathbf{4_c}$. No distinct transitions for $\mathbf{1_g}$ indicated that vesicular $\mathbf{1_v}$ and the (according to cross-polarizing optical microscopy) amorphous crystalline gel strands in $\mathbf{1_g}$ were of different nature. Studies of the presumably involved bilayers with (Fig. 1a) or without (Fig. 1b) interdigitating 'T's' are ongoing to delineate the usefulness of rigid-T vesicles $\mathbf{1_v}$ with

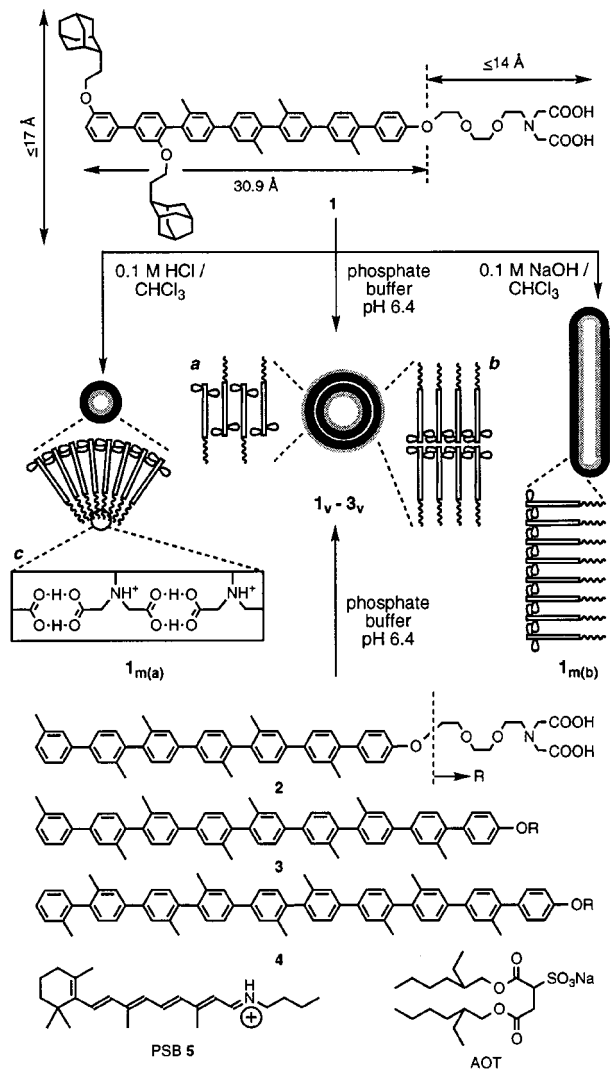

Fig. 1 Structure of oligo(*p*-phenylene)s **1**–**4**, PSB **5**, and AOT; schematic suprastructures for vesicular ($\mathbf{1_v}$–$\mathbf{3_v}$) and micellar ($\mathbf{1_m}$) self-assemblies.

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Table 1 Spectroscopic data for self-assembled amphiphilic oligo(*p*-phenylene)s

	1[a]/Å	Micrographs[b]	λ^{e}_{max}/nm ($\Delta\lambda^{e}_{max}$/nm)[c]	λ^{a}_{max}/nm ($\Delta\lambda^{a}_{max}$/nm)[d]	Hypo.[e]
$\mathbf{1_{m(a)}}$	30.9	Micelles	372 (+2)	288 (−2)	0.70
$\mathbf{1_v}$	30.9	Vesicles	375 (+5)	288 (−2)	0.71
$\mathbf{2_v}$	30.9	Vesicles	386 (+19)	274 (−12)	0.43
$\mathbf{3_v}$	39.4	Vesicles	374 (+9)	276 (−10)	0.53
$\mathbf{4_c}$	43.6	Microcrystals	369 (+2)	258 (−28)	0.20

[a] Calculated length of rigid-rod subunit. [b] SEM, phase-contrast and/or fluorescence microscopy. [c] λ^{3}_{max}: emission maxima, $\Delta\lambda^{e}_{max}$: λ^{e}_{max} of self-assembly − λ^{e}_{max} of monomer in THF. [d] λ^{a}_{max}: absorption maxima, $\Delta\lambda^{a}_{max}$: λ^{a}_{max} of self-assembly − λ^{a}_{max} of monomer in THF. [e] Hypochromism (ε^{a}_{max} of self-assembly/ε^{a}_{max} of monomer in THF).

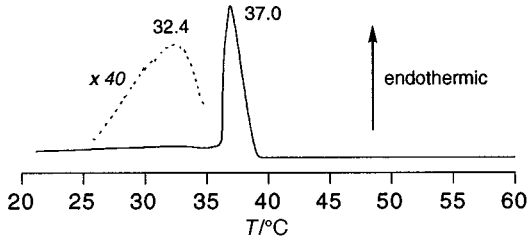

Fig. 2 DSC heating curve of $\mathbf{1_v}$ (scanning rate 1 °C min^{-1}).

T_c = 37.0 °C for applications such as temperature-controlled drug release (Fig. 2).

Optical fluorescence and phase-contrast micrographs contained mainly spherical microparticles for $\mathbf{1_v}$–$\mathbf{3_v}$ and $\mathbf{1_{m(a)}}$ with average diameters that increased with scaffold length and asymmetry ($\mathbf{2_v}$ < $\mathbf{3_v}$ < $\mathbf{1_{m(a)}}$ < $\mathbf{1_v}$, Fig. 3a). Microcrystals were observed for $\mathbf{4_c}$. Perhaps due to better resolution or, more likely, shrinking *in vacuo*, scanning electron microscopy (SEM) revealed nanoparticles for both 'rigid-T' vesicles ($\mathbf{1_v}$, Fig. 3b) and reversed micelles ($\mathbf{1_{m(a)}}$, Fig. 3c). Interestingly, vesicles ($\mathbf{1_v}$) appeared as cavities within precipitated $Na_nH_{3-n}PO_4$ buffer. The additional presence of '8-shaped' besides spherical vesicles implied facile fusion and fission (Fig. 3a/b).

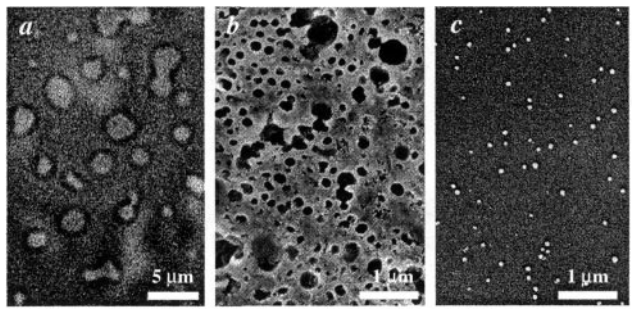

Fig. 3 Representative scanning electron and phase-contrast/fluorescence micrographs for self-assembled **1**–**3**. (a) Fluorescence micrograph for $\mathbf{3_v}$ (diameters: 1.7–3.3 μm). (b) Scanning electron micrograph for $\mathbf{1_v}$ (diameters: 80–260 nm). (c) Scanning electron micrograph for $\mathbf{1_{m(a)}}$ (diameters: 33–73 nm).

Compatibility with the harsh SEM-conditions indicated both stability and high water permeability. The latter was supported for $\mathbf{1_{m(a)}}$ in $CDCl_3$ by a water exchange rate of k = 1.7 ms^{-1} calculated from coalescence of the resonances for intramicellar bulk water (4.78 ppm, ω ([H_2O]/[**1**]) ≈ 100) and extramicellar acidic water (2.18 ppm) at 37.5 °C in the 300 MHz ^{1}H NMR spectra. Extraordinary stability of reversed micelles $\mathbf{1_{m(a)}}$ was further implied by the constant emission intensity of encapsulated HPTS upon dilution of $\mathbf{1_{m(a)}}$. Apparently, the critical micelle concentrations (cmc) of $\mathbf{1_{m(a)}}$ for formation (2 mM) and destruction (< 5 μM) differ significantly. Since rod-shaped **2**–**4** did not self-assemble under identical conditions, the T-shaped structure of **1** seems essential for micellization.[3] However, rapid destruction of $\mathbf{1_{m(a)}}$ by addition of $CuCl_2$, as well as a wormlike morphology for 'basic reversed micelles' $\mathbf{1_{m(b)}}$ (not shown) suggested additional importance of hydrogen bonding in between the hydrophilic iminodiacetate (IDA) termini of **1** for suprastructural organization and stabilization of $\mathbf{1_{m(a)}}$ (Fig. 1c).

Preliminary studies on reversed micelles $\mathbf{1_{m(a)}}$ as biomimetic receptor models revealed that protonated *N*-retinylidene-*n*-butylamine Schiff base (PSB) **5** bound to $\mathbf{1_{m(a)}}$ is not hydrolyzed by intramicellar bulk water.[5] The absorption maximum of PSB **5** surrounded by rigid-rod arene-arrays of the supramolecular host $\mathbf{1_{m(a)}}$ at 456 nm is 16 nm red-shifted compared to that of **5** within conventional AOT reversed micelles.[14] This observation reinforces the potential of $\mathbf{1_{m(a)}}$ as valuable biomimetic receptors. It is in support of the hypothesis that fine-tuning of the absorption of retinylidene Schiff base in bacteriorhodopsins may be governed by aromatic residues in the PSB binding pocket and/or by ring-chain coplanarization of PSB in addition to external point charges.[15]§

In summary, our results imply that single-chain 'rigid-T' amphiphiles are unique surfactants with suprastructural diversity beyond the limitations of comparable rigid-rod amphiphiles. Preliminary results with remarkably stable, water permeable, reversed micelles as biomimetic receptors and catalysts implied potential usefulness of 'rigid-T' amphiphiles in biological, organic and materials chemistry.

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Notes and references

§ The effect of $\mathbf{1_{m(a)}}$ (160 μM in CH_2Cl_2) on the stereoselectivity of cyclopentadiene dimerization (*i.e.* an increasing relative yield of the *exo*-product from 14% to 27%) did not exceed the ordinary influence of reversed micelles.

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