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# Ambidextrous ‘hybrid’ fluorinated zwitterionic geminis: self-assembly in both organic and aqueous media

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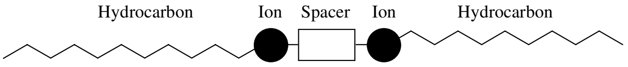
**‘Hybrid’ fluorinated zwitterionic gemini surfactants have been shown to self-assemble in both organic and aqueous media thus being an example of ambidextrous amphiphiles. As a result of these properties, these compounds are attractive targets both from the academic standpoint and in industrial applications.**

The term ‘gemini surfactant’ denotes a class of amphiphilic molecules with a general structure shown below.[1]



Since the name of geminis in 1991, they have been shown to have far superior properties as compared to conventional surfactants, showing up to 100 times lower critical micellar concentrations and significantly improved surface activity. Gemini surfactants have found use in various industrial applications (drug encapsulation, enhanced oil recovery, preparation of high-porosity materials, *etc.*) and have entertained scientific minds in multiple academic research groups due to their ‘unconventional’ behavior and properties.[2]

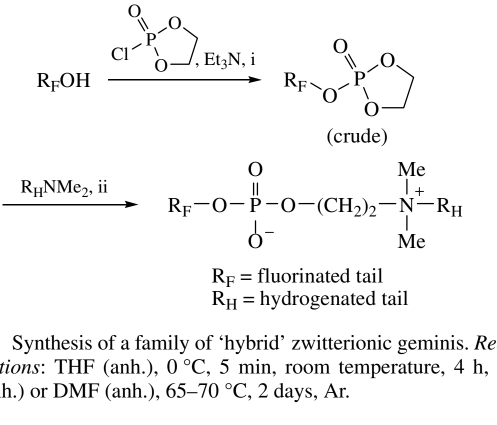
Most of the work in the area of gemini surfactants focused on symmetrical geminis (*i.e.*, both chains and polar groups were identical), and the effects on asymmetry on self-assembly and other properties have not been well understood. One of the first examples of asymmetrical geminis with different chain lengths was reported to be a family of bis(quaternary ammonium) geminis. When dissolved in aqueous media, asymmetrical (*n*-2-*m*) geminis displayed a transition from spherical micelles to various tubular structures depending on the length of the hydrocarbon tails. On the other hand, very asymmetrical geminis formed small spherical micelles only.[3]

In an attempt to gain better understanding of the effect of asymmetry on aggregation properties, we turned our attention towards zwitterionic geminis whose general structure is shown in Scheme 1.[4] The ‘tunability’ of the overall chain length and asymmetry made the zwitterionic geminis attractive candidates for studying aggregation properties as a function of structural variations. Thus, a ‘structural phase diagram’ was constructed (consisting of over 40 geminis with varying hydrocarbon chains) produced some unusual and surprising results: small structural differences led to various morphological changes in water including formation of gels, micelles, coacervates and vesicles.[5]

Intrigued by these findings, we turned our attention to partially fluorinated ‘hybrid’ analogues. The synthesis of ‘hybrid’ zwitterionic gemini surfactants was performed in two steps starting from the appropriate fluorinated alcohols, as shown in Scheme 1. All compounds were fully characterized by NMR ($^1$H, $^{13}$C, $^{19}$F, $^{31}$P), IR, HRMS and EA and appeared as white hygroscopic solids soluble in alcoholic and halogenated solvents.

Examples of synthesized compounds along with their respective abbreviated symbols (which should be self-explanatory) are shown in Scheme 2 and include $F_8C_2$–$C_{14-22}$; $F_6C_2$–$C_{14-22}$; $F_7C_1$–$C_{14-22}$; $HF_6C_1$–$C_{14-22}$; $HF_4C_1$–$C_{14-18}$; $F_6C_2$–$C_{8-12}$; $F_7C_1$–$C_{8-12}$; $HF_6C_1$–$C_{8-12}$. Note that the fluorinated chains are always on the phosphate side of the geminis.

When $F_6C_2$–$C_{18}$ was hydrated with water (electroformation method),[6] giant unilamellar vesicles were formed [Figure 1(*a*)]. Formation of vesicles from these amphiphiles in water was expected if past hydrocarbon analogues were any guide. However, to our surprise, when $F_6C_2$–$C_{18}$ was smeared on the microscope slide followed by immersion in toluene, long bilayer tubules (reminiscent of myelin figures formed upon hydration of phospholipids) were observed, as shown in Figure 1(*b*). To ensure reproducible preparations, smeared solids were necessary to expose to a mist of water or high relative humidity (> 70% RH) for a few minutes prior to addition of an appropriate organic solvent (cyclohexane, hexane, toluene, chlorocyclohexane or dodecane). It is quite important for the solid gemini to be ‘prehydrated’ before organic solvent is added. Thus, if an organic solvent was added to a dry solid, then only a few tubules were observed. On the other hand, if a solid gemini was ‘prehydrated’ prior to the treatment with an organic solvent, a large number of tubules were reproducibly observed. Thus, $F_6C_2$–$C_{18}$ can be called an ambidextrous amphiphile; *i.e.*, it aggregates into bilayer assemblies in both aqueous and non-polar organic media. Bilayer morphologies were obtained with several other geminis including $F_8C_2$–$C_{14-22}$; $F_6C_2$–$C_{14-22}$; $F_7C_1$–$C_{14-22}$; $HF_6C_1$–$C_{14-22}$; $HF_4C_1$–$C_{14-18}$. When a water-soluble dye (Lucifer Yellow) was sprayed onto to $F_6C_2$–$C_{20}$ followed by addition of cyclohexane,



**Scheme 1** Synthesis of a family of ‘hybrid’ zwitterionic geminis. *Reagents and conditions*: THF (anh.), 0 °C, 5 min, room temperature, 4 h, Ar; ii, MeCN (anh.) or DMF (anh.), 65–70 °C, 2 days, Ar.

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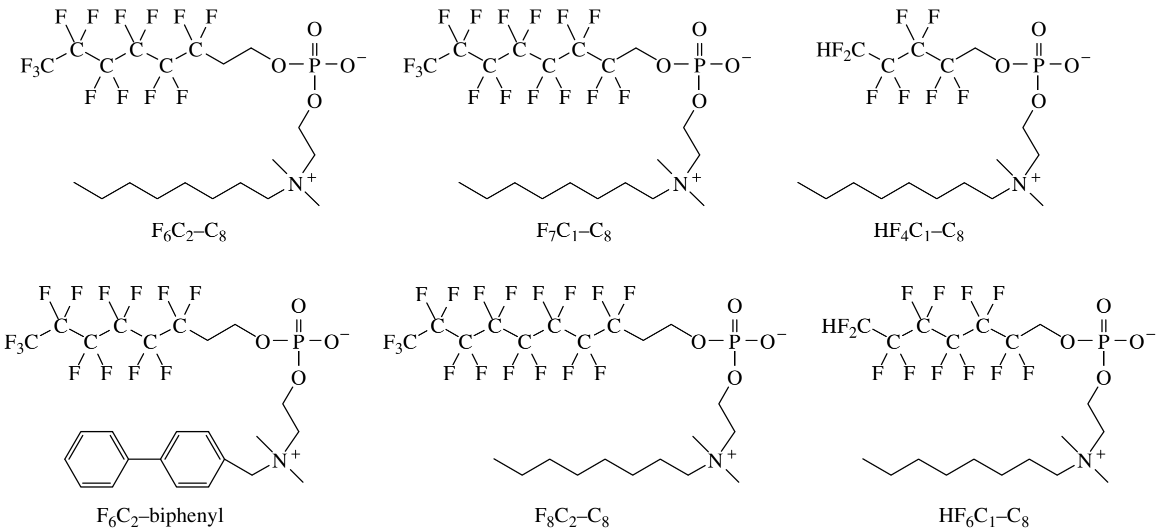

**Scheme 2** Examples of ‘hybrid’ fluorinated geminis.

a large number of vesicular structures was produced with fluorescence concentrated at the periphery of the aggregates, demonstrating that water either creates a thin layer or the dye concentrates around the polar heads of the geminis [Figure 1(*c*)].

The observed aggregates appear to be reminiscent of the reversed vesicles initially observed by Kunieda *et al.* from tetraethyleneglycol dodecyl ether mixed with 89% dodecane and 9% water.[7] It was found later that reversed vesicular systems can be produced by a variety of surfactants and their mixtures, *i.e.*, Aerosol OT–SDS–decane–water,[8] lecithin–squalane–water, glycerol monolauryl ether–$N^{\alpha}$-lauroyl arginine methyl ester hydrochloride (LAM), hexanol–lysolecithin,[9] sucrose monoalkanoate (DKE)–hexanol–water–decane,[10] DKE–hexaethyleneglycol hexadecyl ether–decane–water,[11] DKE–isooctane–water,[12] polyoxyethylene(50.8) oleyl ether–*m*-xylene–water.[13] The basis of reversed vesicle formation has been examined, and it was determined that a combination of a hydrophilic surfactant with a lipophilic oil-soluble compound was essential for the formation of reversed vesicles. More relevant to our system, the presence of a small amount of water is usually necessary to, presumably, solvate the polar groups.

‘Hybrid’ fluorinated geminis do not require addition of other molecules or any significant amounts of water. The following observations can be deduced. (*a*) Reversed vesicles are formed in non-polar organic solvents if the hydrogenated chain is longer than 14 carbons. The shorter the hydrocarbon chain, the less the solubility of the resulting geminis in organic solvents[‡] and the poorer the compatibility with oil. For example, $F_8C_2$–$C_{14-22}$, $F_6C_2$–$C_{14-22}$, $F_7C_1$–$C_{14-22}$, $HF_6C_1$–$C_{14-22}$ and $HF_4C_1$–$C_{14-18}$ produced reversed vesicles and tubules, while $F_6C_2$–$C_{8-12}$, $F_7C_1$–$C_{8-12}$ and $HF_6C_1$–$C_{8-12}$ showed no signs of aggregation in non-polar organic solvents including cyclohexane, hexane, toluene, chlorocyclohexane, and dodecane. (*b*) The fluorinated chain is an essential ‘ingredient’ for the formation of reversed vesicles as no reversed vesicles were observed with totally hydrogenated geminis under the conditions studied. This important observation demonstrates that there is some additional stabilization of reversed vesicles caused by the presence of a fluorinated chain, which is solvophobic in hydrocarbon media. (*c*) No aggregation was observed in fluorocarbons, indicative of insufficient stabilization of the hypothetical bilayers by a single hydrocarbon chain. (*d*) Exchange of a hydrocarbon tail with a biphenyl group ($F_6C_2$-biphenyl) did not result in the formation of reversed vesicles.

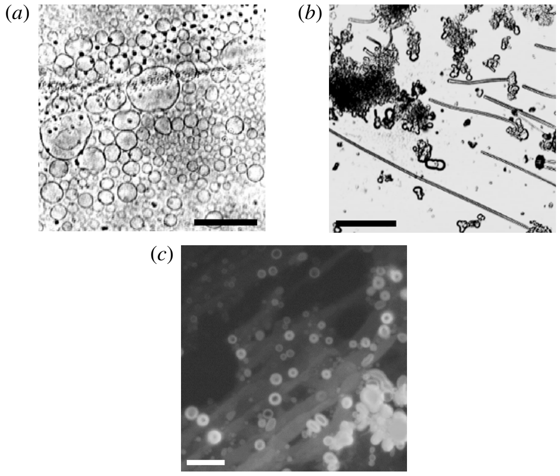

**Figure 1** (*a*) Vesicles from $F_6C_2$–$C_{18}$ in water, prepared by the electroformation method (see supporting information, bar = 60 μm). (*b*) Tubular structures of $F_6C_2$–$C_{18}$ in toluene (bar = 140 μm). (*c*) Fluorescent images of reversed vesicles from $F_6C_2$–$C_{20}$ in cyclohexane (bar = 40 μm).

Likely owing to the solvophobic nature of the fluorinated chain, the ‘hybrid’ geminis were noticed to have some unusual properties in supercritical $CO_2$ making these compounds potentially attractive for use in dry cleaning applications.[14] Before this happens, however, a great deal more must be learned about the physico-chemical properties of these unusual, but rather easily prepared, variations on the gemini theme.

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*Online Supplementary Materials*

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.mencom.2007.03.009.

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