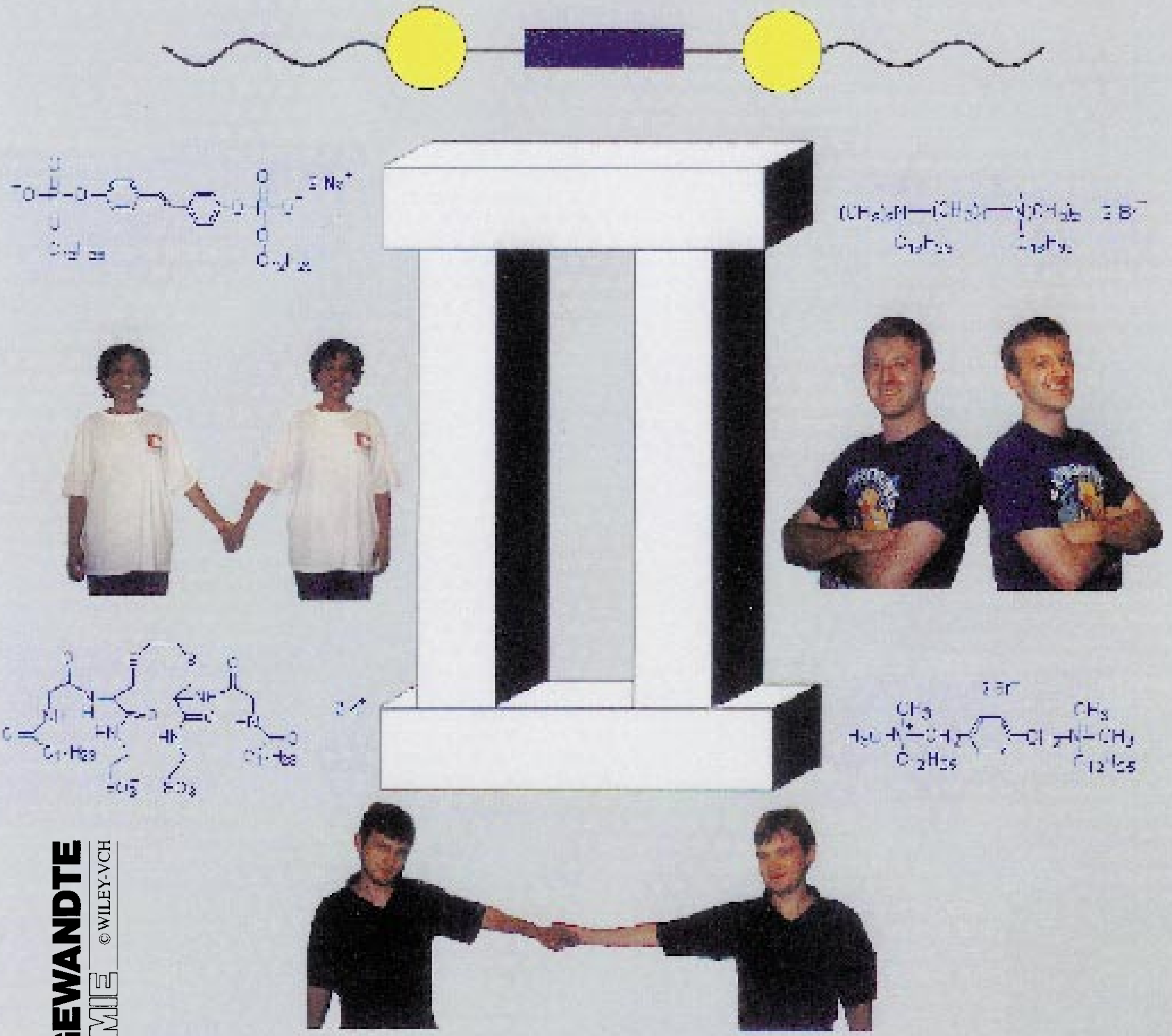
Gemini Surfactants



ANGEWANDTE CHEMIE

General structure (top), four examples of gemini surfactants, and three (six?) Emory graduate students working in the field of geminis:
Bessie Mbadugha (left), Kevin Caran (right), and Andrey Peresypkin (bottom).

Gemini Surfactants

Fredric M. Menger* and Jason S. Keiper

How easy it is to dismiss the humdrum surfactant! After all, its structure is unglamorous by present-day norms. And the surfactant has been entrenched in so many areas of commerce for so many decades that its chemistry might seem old and tired. The purpose of this review is to persuade the reader otherwise, all the while focusing on a remarkable new surfactant, the gemini. Geminis, the common name for "bis-surfactants", can self-assemble at concentrations almost a hundredfold lower than for corresponding conventional surfactants. Surface activity can be improved a thousandfold. Geminis have already shown promise in skin care, antibacterial regimens, construction of high-porosity materials, analytical separations, and solubilization processes. Scores of patents dealing with geminis have appeared in the last few years. Indeed, geminis might well turn out, in the opinion of some, to be more useful to "l'homme de la rue" than crown ethers or fullerenes. This review delves into such topics as synthesis, critical micellization concentration, aggregate size and shape, gels, vesicles, and films. The information comes from scientists all over the world; one might say that gemini research is bathed in a continuous sunlight or summer. No prior knowledge of colloid chemistry is presupposed in this article.

Keywords: colloids · micelles · surface chemistry · surfactants

1. Introduction

One of the last things chemistry needs is new and superfluous terminology. We felt justified in coining the expression "gemini surfactant" only because geminis have structures and properties that are unique to the world of surfactants.[1, 2] Thus, a conventional surfactant has a single hydrocarbon tail connected to an ionic or polar headgroup. In contrast, a simple gemini has the arrangement shown in Figure 1. A specific example would be $C_{12}H_{25}N^+(CH_3)_2{-}CH_2{-}C_6H_4{-}CH_2{-}N^+(CH_3)_2C_{12}H_{25}$. Actually, related surfactants with more than two tails are now known, and we have absorbed them into the gemini classification even though this creates something of a misnomer. As far as the unique properties are concerned, geminis can be orders of magnitude more surface-active than comparable conventional surfactants.[3] And apparent critical micellization concentrations (where surfactants abruptly aggregate in water) can be larger for longer chains than for shorter chains (just the reverse of normal).[2] It is the purpose of this review to inform the general reader about a remarkable set of compounds.

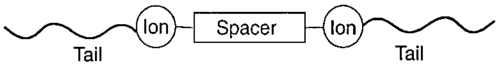


Figure 1. Schematic representation of the gemini surfactant structure.

Before proceeding, things should be clarified historically. In 1991 we assigned the word "gemini" to bis-surfactants in which the spacer is rigid (e.g. a benzene or stilbene system).[1] The idea was to examine how enforced separation of the two hydrocarbon chains within a surfactant molecule would affect its properties. It was only later that others extended the definition to include all such double-surfactants regardless of whether the spacers were rigid or not. The point here is that, under this more general definition, geminis were known long before our own entry in the area. Special mention should be made of Bunton et al., who studied the catalysis of nucleophilic substitutions by "dicationic detergents";[4] of Devinsky et al., who reported on the surface activity and micelle formation of some new "bisquaternary ammonium salts";[5] and of Okahara et al., who prepared and examined "amphipathic compounds with two sulfate groups and two lipophilic alkyl chains".[6]

How quickly these days the summarizable becomes the unsummarizable! In the last half-dozen years, interest in geminis has soared and, along with it, so has the publication rate. Rosen and Tracy, in a particularly readable account appearing in a 1998 issue of *Journal of Surfactants and Detergents*, list over 60 journal articles and nearly 40

---

[*] Prof. Dr. F. M. Menger, J. S. Keiper
Department of Chemistry
Emory University
Atlanta, GA 30322 (USA)
Fax: (+1) 404-727-6586
E-mail: menger@emory.edu

patents.[7] (Our own work, having been supported by two public agencies, the NIH and NSF, was never patented.) In front of us is a stack of virtually all papers on geminis. The nations from which the authors hail are the following: France (36); USA (25); Japan (21); India (11); Germany, Israel, The Netherlands, and Spain (7); Slovakia (6); United Kingdom (5); New Zealand (4); Italy (3); Belgium and Russia (2); Argentina, Greece, and Sweden (1). Adolf Wurtz once remarked that chemistry is a French science, and when it comes to gemini chemistry it must be admitted his country has played a leading role. However, we prefer to take a more global view and express pleasure that gemini research is an activity which is never denied sun nor summer.

A disadvantage of our particular style of review is that some contributors to the field are not mentioned and are, therefore, owed an apology. It may be only scant compensation that within our cited papers there appear reference lists that, taken collectively, include everybody's work.

2. Structure

The first task is to give a representative sampling of gemini structures that have already been synthesized, and Scheme 1 serves that purpose. Relevant structural features, many of which are illustrated in Scheme 1, include:

a) All geminis possess at least two hydrophobic chains and two ionic or polar groups.
b) A great deal of variation exists in the nature of the spacer, which can be short (2 methylene groups) or long (12 methylene groups); rigid (stilbene) or flexible (methylene chain); and polar (polyether) or nonpolar (aliphatic, aromatic).
c) The polar group can be positive (ammonium), negative (phosphate, sulfate, carboxylate), or nonionic (polyether, sugar[18]).
d) Although the great majority of geminis have two identical polar groups and two identical chains, unsymmetric geminis are known.[15, 19]
e) "Geminis" with three or more polar groups or tails have been synthesized.[20–23]

One can appreciate, from a brief inspection of Scheme 1, how colloid chemistry, for so long confined to conventional and commercially available surfactants, has been able to expand its outlook with fresh new possibilities.

3. Synthesis

Before physical characterization of a gemini can begin, the compound must, of course, be synthesized. Understandably, this is an impediment for those who are not inclined toward synthetic organic chemistry. Two factors ameliorate the problem. First, gemini synthesis and purification, while sometimes not trivial, are also not tedious by present-day standards. Second, those who are repelled by synthesis can often seek help from those who are not. We (meaning the students of Emory who seem to enjoy synthesis) have prepared over one hundred geminis, many of which have been sent worldwide to academic and industrial laboratories alike. (We are especially pleased when receipt of requested compounds is acknowledged with a brief letter of thanks.) Fruitful collaborations between groups of different expertise are common in the gemini arena.

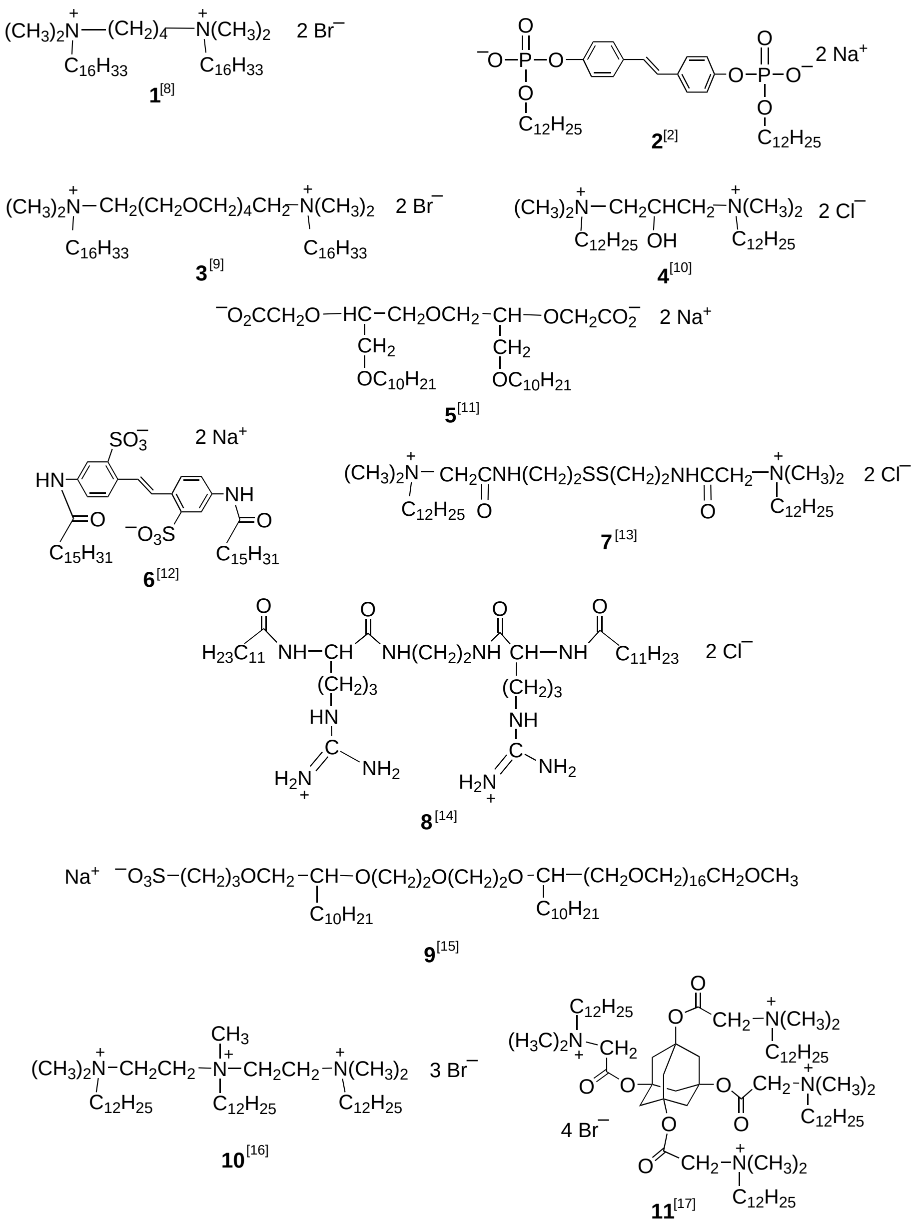
Simple cationic geminis, $RN^+(CH_3)_2-(CH_2)_n-N^+(CH_3)_2R$ ($R =$ a long chain) can be prepared as shown in Scheme 2 either by method A or B (with method B being preferable when $n = 2$). Typically, one boils under reflux a mixture of the reagents in dry ethanol for two or three days and purifies the product by recrystallization.[8] Method A is attractive when the dibromide is reactive and commercially available (e.g. $BrCH_2C_6H_4CH_2Br$ to create an aromatic spacer).[2] If the


F. M. Menger (on the right)

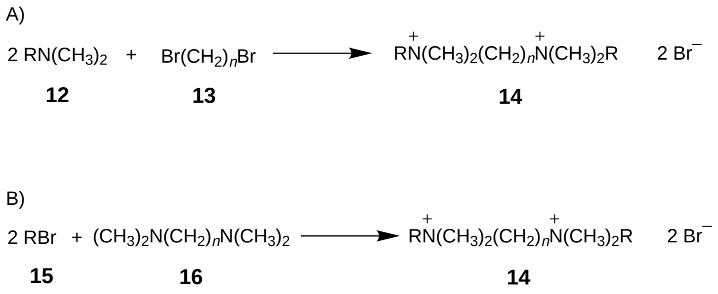

J. S. Keiper

Fredric M. Menger is the author of two previous reviews in Angewandte Chemie incorporating his group's other research interests in self-assembling systems and giant vesicles. He received his B.A. from the Johns Hopkins University in 1958 and his Ph.D. from the University of Wisconsin in 1963. He subsequently was Postdoctoral Research Fellow at the Northwestern University (1963–1965). A list of publications and his scientific credentials can be found on the Internet (http://www.emory.edu/CHEMISTRY/faculty/menger.html). Rather unknown are his diversions from the stress of chemical research: mountain climbing (the first American to ascend the highest peak in Russia); music (blues harmonica under a pseudonym); field work (water and road projects in Nicaragua); and biology (a forthcoming book on the evolution of the mind).

Jason S. Keiper is a graduate student in Professor Menger's group at Emory University. After this he will be pursuing postdoctoral studies with Professor Joseph DeSimone at the University of North Carolina. His interest in colloid chemistry was sparked during undergraduate work with Professor Larry Romsted at Rutgers University. While surfactants and lipids occupy the majority of his time, he finds solace in his tenor saxophone and stock cars.



Scheme 1. Representative sampling of gemini structures that have already been synthesized.



Scheme 2. Synthesis of simple cationic geminis. Method B is preferred when $n = 2$.

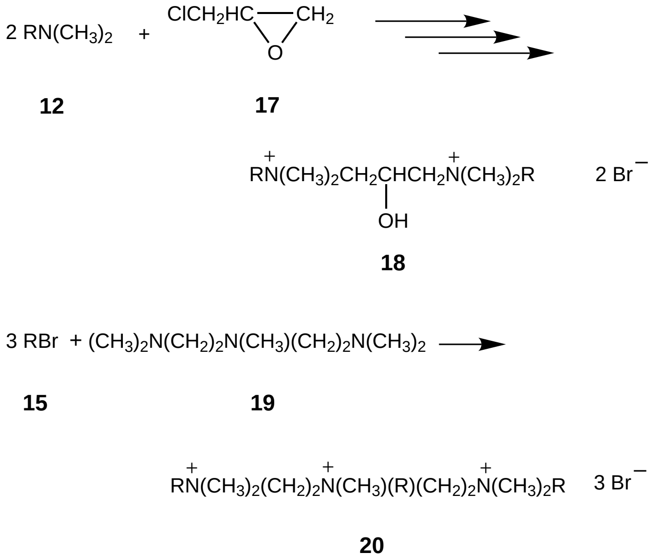
dibromide is not purchasable, then it might be possible to synthesize it from the corresponding dialcohol (e.g. $HOCH_2(CH_2OCH_2)_3CH_2OH$ plus PBr_3 gives $BrCH_2(CH_2OCH_2)_3CH_2Br$ and, from there, a gemini with a polyoxyethylene spacer).[9] Variations on these themes are shown in the top part of Scheme 3; an alkylation of the tertiary amine occurs at the less substituted epoxide carbon atom, leading to **18**.[10] A specific example of Method B is shown in the preparation of "trimeric" gemini **20**; over 40 h in 1-propanol at 100 °C, followed by column chromatography, were required for this reaction.[22]

Anionic gemini **22**, a bis-phosphodiester with a flexible spacer, has been synthesized as detailed in Scheme 4 using well established chemistry.[24] Synthesis of the corresponding gemini with a rigid stilbene spacer, **2**, also involved a multistep but routine procedure.[2]

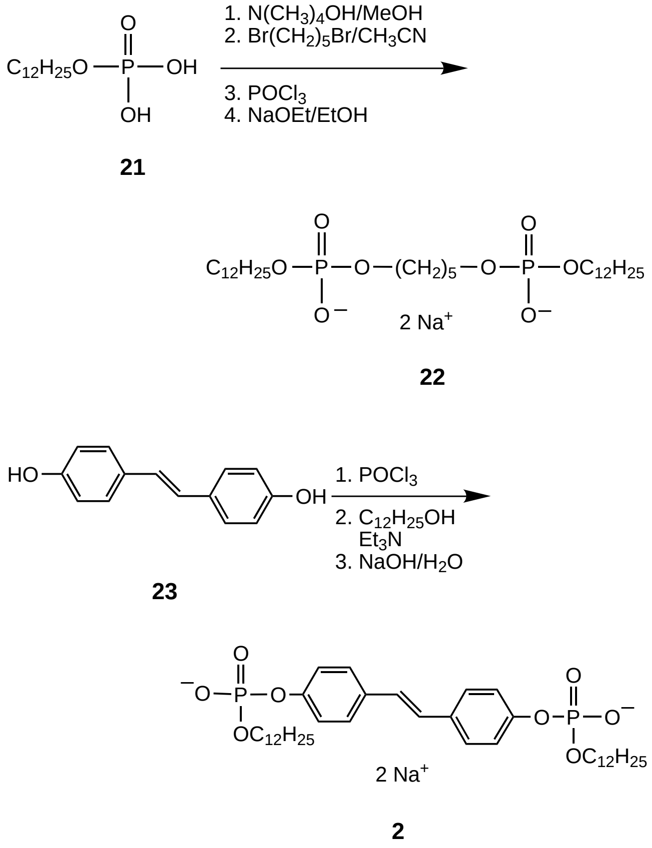
Geminis can be as complex as the desires and ambitions of the investigator allow. Four examples of more intricate geminis are given in Schemes 5–8. No particular lesson is intended here except, perhaps, that synthetic chemistry provides an opportunity for the colloid chemist to explore structure–activity relationships that are otherwise beyond reach. Virtually all known analytical methods have already been applied to micellar systems composed of conventional surfactants. This mode of research, milked to exhaustion, is being revived with wonderful new structures. To illustrate the diversity made possible through synthesis, we might mention a recently obtained gemini-type surfactant with four ionic groups and four chains tetrahedrally disposed about an adamantane nucleus (compound **11** in Scheme 1).[17] At the time of this writing, we have no data, and few premonitions, concerning the colloidal properties of such a molecule. As with all surfactants, the purity of the geminis is of critical concern. This concern is reflected, for example, in diphosphate geminis (e.g. **2**), which we characterized by NMR spectroscopy (^1H, ^{13}C, ^{31}P), mass spectrometry (FAB), and elemental analysis.[2] Single ^{31}P NMR signals were particularly satisfying indications of purity.

4. Critical Micellization Concentration

The colloid chemist has a host of experimental options when contemplating the characterization of a newly acquired surfactant: calorimetry, conductometry, ESR spectroscopy, goniometry, microscopy, light scattering, neutron scattering, NMR spectroscopy, rheometry, spectrophotometry, and ten-

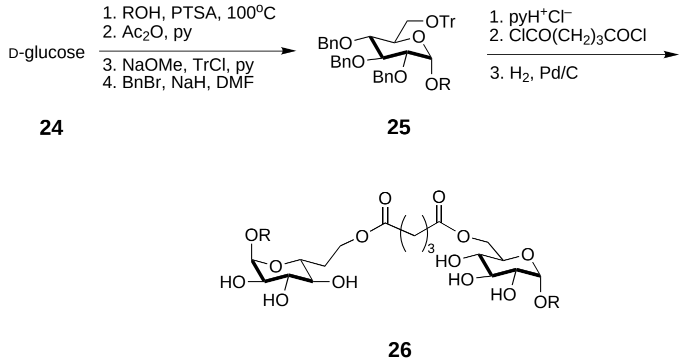


Scheme 3. Top: A variation to methods A and B (Scheme 2) for the synthesis of cationic geminis.[10] Bottom: A specific example of method B for the synthesis of **20**.[22]

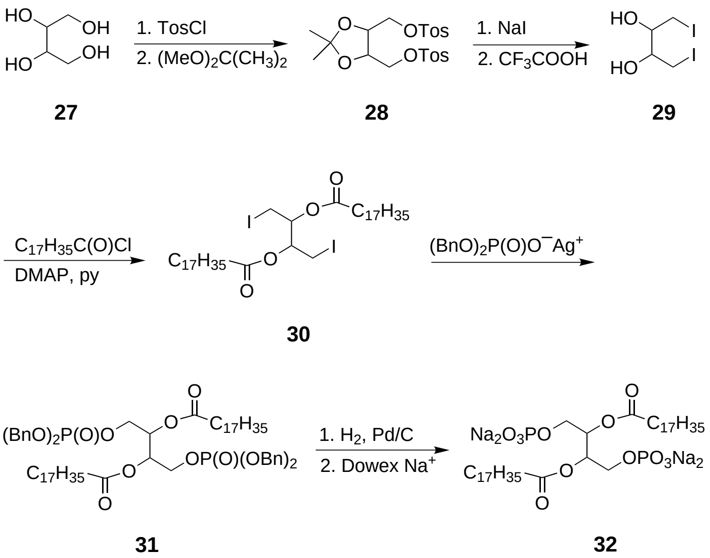


Scheme 4. Synthesis of **22**[24]and **2**.[2]

siometry to name a few. Information is thereby acquired on micelle formation and structure, surface activity, solubilization, adsorption, wetting, foaming, phase behavior, and thermotropic properties. One parameter, however, stands out as the mainstay, the keystone of all surfactant research: the critical micellization concentration (CMC). The CMC is the concentration above which monomeric surfactant molecules abruptly assemble into aggregates called micelles. "Abruptly" is, of course, a subjective term. If the micelles are small (e.g. 10 molecules), then the CMC may embody a concentration range. If, on the other hand, the micelles are a more usual size of 50–100 molecules, then the CMC is indeed sharply defined owing to the highly cooperative nature of the aggregation process. In any event, the CMC is useful in that it reveals the propensity of the surfactant to assemble in water. For example, it stands to reason that the longer a surfactant's tail, the lower its CMC. Hydrophobic forces, opposed by electrostatic repulsion among the ionic headgroups at the micelle surface, drive the micellization. Micelles are known to be disorganized assemblies with interiors consisting of mobile, nonlinear hydrocarbon chains.[28]

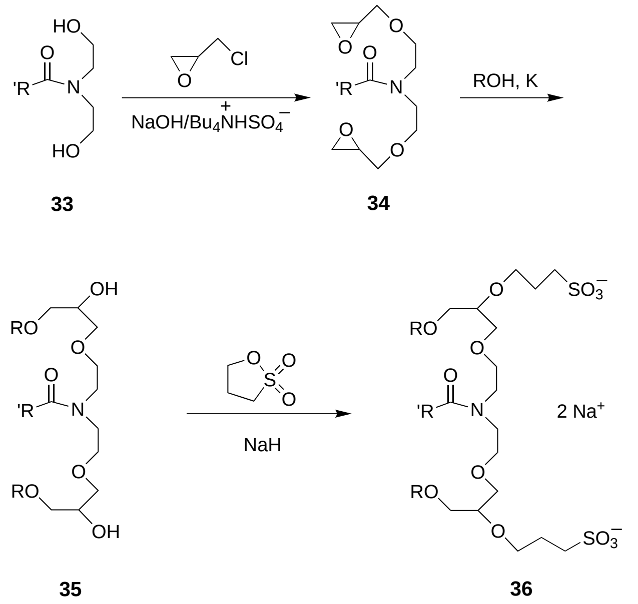


Scheme 5. Synthesis of **26**.[18] The authors carried out the synthesis with R = butyl, but the sequence is applicable to longer chains as well. Bn = benzyl, PTSA = *p*-toluenesulfonic acid, py = pyridyl, Tr = triphenylmethyl (trityl).



Scheme 6. Synthesis of **32**.[25] Three stereoisomers of the product (*R*,*R*, *S*,*S*, and *R*,*S*) were prepared. Tos = toluene-4-sulfonyl.

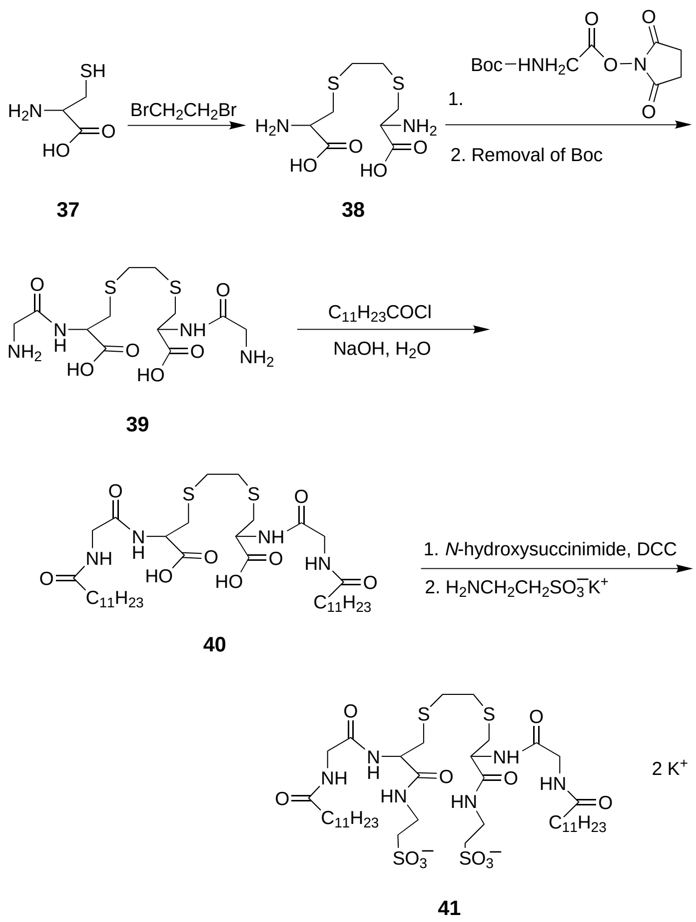
Surface tension is probably the most common means of determining the CMC. Below the CMC, surfactant molecules position themselves at the air/water interface and thus lower the surface tension. Above the CMC, any added surfactant prefers to join a micelle rather than to enter the interfacial film. Consequently, a plot of surface tension versus concentra-



Scheme 7. Synthesis of **36**.[26] Double- or triple-chained surfactants were prepared depending on whether R′ was short (CH_3) or long ($C_{11}H_{23}$) while keeping R long ($C_{10}H_{21}$).

tion decreases steeply below the CMC and levels off above it; the break in the plot is taken as the CMC.[29] The method is fast, convenient, and nondestructive to the surfactant. The only cautionary note is that surface tension can be time-dependent, so that it is often advisable to make measurements on samples that have rested undisturbed for many hours.[2]

Table 1 lists CMC values for 14 geminis (preceded by four conventional surfactants for comparison purposes). Depending upon how the data were obtained, CMCs can differ by twofold or more, but such an uncertainty is insignificant relative to the large variations evident. Interesting generalizations emerge from the numbers:



Scheme 8. Synthesis of **41**.[27] Boc = *tert*-butoxycarbonyl, DCC = *N,N′*-dicyclohexylcarbodiimide.

a) Geminis have remarkably low CMC values compared with corresponding surfactants of equivalent chain length. (The comparison is, justifiably, made on a "per ionic headgroup" basis while neglecting the spacer.) For example, the CMC in entry 5 is 16 times smaller than in entry 1, and the CMC in entry 18 is 80 times smaller than in entry 4.

Table 1. Critical micellization concentrations (CMC) of representative gemini surfactants.[a]

Entry	Surfactant	CMC [mM]	Ref.
1	$C_{12}H_{25}N^+(CH_3)_3\ Br^-$	16	[7]
2	$C_{12}H_{25}N^+(CH_3)_3\ Cl^-$	22	[20]
3	$C_{16}H_{33}N^+(CH_3)_3\ Br^-$	1	[30]
4	$C_{12}H_{25}OSO_3^-\ Na^+$	8	[7]
5[b]	$C_{12}H_{25}N^+(CH_3)_2{-}(CH_2)_n{-}N^+(CH_3)_2C_{12}H_{25}\ 2\,Br^-$	1	[31]
6	$C_{12}H_{25}N^+(CH_3)_2{-}(CH_2)_{16}{-}N^+(CH_3)_2C_{12}H_{25}\ 2\,Br^-$	0.12	[8]
7	$C_{16}H_{33}N^+(CH_3)_2{-}(CH_2)_2{-}N^+(CH_3)_2C_{16}H_{33}\ 2\,Br^-$	0.003	[32]
8	$C_8H_{17}N^+(CH_3)_2{-}(CH_2)_3{-}N^+(CH_3)_2C_8H_{17}\ 2\,Br^-$	55	[33]
9	$C_{12}H_{25}N^+(CH_3)_2{-}(CH_2)_2{-}O{-}(CH_2)_2{-}N^+(CH_3)_2C_{12}H_{25}\ 2\,Cl^-$	0.5	[7]
10	$C_{16}H_{33}N^+(CH_3)_2{-}(CH_2)_5{-}N^+(CH_3)_2C_{16}H_{33}\ 2\,Br^-$	0.009	[34]
11	$C_{16}H_{33}N^+(CH_3)_2{-}(CH_2)_2{-}O{-}(CH_2)_2{-}N^+(CH_3)_2C_{16}H_{33}\ 2\,Br^-$	0.004	[34]
12	$C_{16}H_{33}N^+(CH_3)_2{-}CH_2{-}(CH_2{-}O{-}CH_2)_3{-}CH_2{-}N^+(CH_3)_2C_{16}H_{33}\ 2\,Br^-$	0.02	[9]
13	$C_{12}H_{25}N^+(CH_3)_2{-}CH_2{-}CH(OH){-}CH_2{-}N^+(CH_3)_2C_{12}H_{25}\ 2\,Br^-$	0.8	[10]
14[c]	$C_{12}H_{25}N^+(CH_3)_2{-}CH_2{-}C_6H_4{-}CH_2{-}N^+(CH_3)_2C_{12}H_{25}$	0.03	[29]
15	$C_{12}H_{25}N^+(CH_3)_2{-}CH_2{-}CH(OH){-}CH(OH){-}CH_2{-}N^+(CH_3)_2C_{12}H_{25}\ 2\,Br^-$	0.7	[35]
16	$C_{12}H_{25}N^+(CH_3)_2{-}CH_2{-}CH(OH){-}CH_2{-}N^+(CH_3)_2{-}CH_2{-}CH(OH){-}CH_2{-}N^+(CH_3)_2C_{12}H_{25}\ 3\,Cl^-$	0.5	[36]
17	$C_{12}H_{25}OPO_2^-{-}O{-}(CH_2)_6{-}O{-}PO_2^-OC_{12}H_{25}\ 2\,Na^+$	0.4	[34]
18	$C_{10}H_{21}O{-}CH_2{-}CH(OSO_3^-){-}CH_2{-}O{-}(CH_2)_2{-}O{-}CH_2{-}CH(OSO_3^-){-}CH_2{-}OC_{10}H_{21}\ 2\,Na^+$	0.01	[37]

[a] Entries 1–4 list conventional surfactants for comparison purposes. [b] $n = 3–8$. [c] In 0.1 N NaCl.

b) The CMC values are not sensitive to the polarity of short spacers (2 – 8 atoms). Attention is called to the C_{12} geminis in entries 5, 9, 13, 15, and 16, all with diverse spacers but with CMC values within a factor of 2 of each other.
c) A long hydrocarbon spacer of 16 methylene groups reduces the CMC almost tenfold relative to a short spacer of 3 – 8 methylene groups (compare entries 5 and 6). No doubt the long spacer contributes to the overall hydrophobicity of the gemini, reducing the monomer solubility and enhancing its tendency to self-assemble.
d) Geminis are more responsive to tail length than conventional surfactants. Thus, increasing the tail length by four carbon atoms in a conventional cationic surfactant lowers the CMC 16-fold (entries 1 and 3). A corresponding tail lengthening in the gemini series lowers the CMC by two orders of magnitude (compare entries 5, 7, and 10).
e) Other factors being more or less equal, anionic surfactants have somewhat lower CMC values than their cationic counterparts (compare entries 5 and 17).

5. Aggregation Numbers

A critical micellization concentration says nothing about the size or shape of a micelle. One suspects that gemini micelles are not of the small, "5 – 10 monomer" variety because plots of surface tension versus concentration show a sharp bend at the CMC.[35] Small micelles would have produced a broad transition region. In any event, the question can be settled by determining the number of molecules per micelle (i.e., the aggregation number or AN) using one of several methods: light or neutron scattering and steady-state or time-resolved fluorescence quenching. Since light scattering according to P. Debye is tedious and requires extrapolation to low concentrations (owing to interfering micelle – micelle interactions), current use of the method is rare.[38] Neutron scattering is more common but costly and not generally available. This leaves fluorescence methods involving a probe (often pyrene) and an appropriate quencher. Steady-state fluorescence quenching is especially popular, and it merits a brief description.

In the steady-state fluorescence method, one measures the emission of a probe (whose concentration is much smaller than the concentration of the micelles, [M]) as the quencher concentration, [Q], is increased from 0 to about twice that of the micelles. An ordinary spectrofluorometer works fine.[39] The major assumptions are a) the probe fluorescence lifetime is much shorter than the residence times of the probe and the quencher within the micelle; b) quenching is much faster than probe decay; and c) Poisson statistics control the distribution of probe and quencher among the micelles. Under these circumstances, the delightfully simple Equation (1) is obeyed (where I_O and I_Q are the fluorescence emission in the absence and presence of quencher, respectively).

$$\frac{I_O}{I_Q} = \exp\left(\frac{[Q]}{[M]}\right) \tag{1}$$

By plotting $\ln(I_O/I_Q)$ versus [Q] at a constant total concentration of surfactant, $[S]_{total}$, one obtains the concentration of the micelles. Assuming that the concentratin of the surfactant monomer at all times equals the CMC, then the AN can be calculated from Equation (2) for which all three terms to the right of the equal sign are now known.

$$\mathrm{AN} = \frac{[S]_{total} - \mathrm{CMC}}{[M]} \tag{2}$$

Before specifying AN values, it will be helpful to introduce a shorthand notation for the cationic geminis. A gemini with two C_{12} tails and a C_3 spacer separating the quaternary nitrogen atoms (see entry 5 in Table 1) will, for example, be designated 12-3-12. The AN for 12-3-12 is 45 (determined by pyrene fluorescence quenching at 0.02 M surfactant).[39] Small-angle neutron scattering data gave AN values of 35 and 74 for 10-3-10 (1 wt%) and 16-5-16 (2.5 mM), respectively.[40, 41] Gemini micelles tend to expand at increased concentrations, with 16-5-16 growing from 74 at 2.5 mM to 138 at 50 mM.[42] Of course, just as the CMC says nothing about the AN, the AN reveals little about micelle shape. This latter topic is covered in Section 6. For the moment it is sufficient to know that gemini aggregation numbers (as far as they are known) are usually not out of the ordinary relative to those of single-chained analogues.

6. Micelle Shape

Micelle shape is a complicated business, as it depends not only on surfactant structure but also upon solution conditions such as concentration, temperature, and ionic strength. Yet despite its complexities, shape is worth discussing because it affects rheological and solubilization properties, which are important issues from a practical standpoint. Spherical micelles, formed by many conventional surfactants at moderate concentrations, are favored by large headgroups which impair orderly packing. If there are two chains per headgroup, as in a phospholipid, then the headgroup and chains are of roughly equal diameter and the compound can pack into a parallel array (i.e., a bilayer). In addition to spherical micelles, one finds shapes that are oblate (disklike) or prolate (like a medicine capsule or rod). Nonspherical micelles can be formed even by single-chained surfactants; cetyltrimethylammonium bromide above 0.2 M, for example, assembles into micelles with an elongated shape.[43]

Small-angle neutron scattering indicates that 16-3-16 at 2.5 – 10 mM and 30 °C forms disklike micelles.[44] Upon heating to 45 – 70 °C, the disk converts into a rod (with a length of 500 Å and a radius of 27 Å) owing, probably, to subtle changes in the effective charge per monomer. With spacers of 5 or longer, micelles are prolate-shaped. Thus, spacer length controls micelle shape more than it does CMC. In summary, 16-3-16 behaves as if its headgroup were unusually small since the spacer is shorter than the equilibrium distance between charged headgroups within a conventional micelle; more orderly packing is thus possible. When a spacer length is increased to 5 and above, the effective headgroup area increases to a relatively normal value, and the micelle rearranges its shape closer to that assumed by a cetyltrimethylammonium bromide micelle.

Cryo-transmission electron microscopy studies on 12-*n*-12 and 16-*n*-16 geminis have produced photos with the following morphologies: a) giant, entangled, wormlike micelles with 12-2-12 and 12-3-12 (consistent with an observed viscoelasticity at higher concentrations); b) spherical micelles for 12-*n*-12 ($n = 4$, 8, 12); c) vesicles of 12-16-12; d) vesicles, membrane fragments, and wormlike micelles for a sample of 16-3-16 prepared from a 12 mM solution.[45] This last observation is somewhat worrisome as it conflicts with the results from small-angle neutron scattering (SANS). Since both cryo-electron microscopy (cryo-EM) and SANS entail assumptions and/or potential artifacts, the source of the discrepancy is unclear.

In the absence of any added salt, solutions of less than 2 wt% 12-2-12 display low viscosities. Above 2 wt%, however, the viscosity rises abruptly due to formation of wormlike micelles.[46] The average length of the worms, and hence the viscosity, is affected by two opposing forces: a) electrostatic repulsive energy among the cationic nitrogen atoms that favors scission of the worms; and b) "end-cap energy" that favors micelle growth by minimizing the number of high-energy termini. At elevated 12-2-12 concentrations, electrostatic interactions become screened, end-cap energy assumes a more dominant role, and the micelles grow into semiflexible worms. It is interesting that micelles can be forced to grow even at lower 12-2-12 concentrations by an applied shear that exceeds a certain critical shear rate.[47] The tendency to form worms increases as the spacer length decreases and the chain length decreases.

Attention should be drawn to theoretical modeling of ionic and nonionic geminis, with both hydrophobic and hydrophilic spacers, using Monte Carlo simulations.[48] Among the various conclusions, we cite the following:

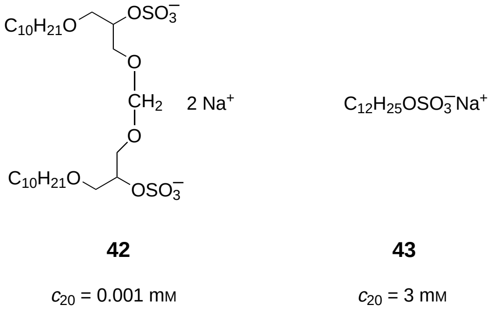
a) Short hydrophobic spacers give grossly nonspherical micelles ("threads"), whereas long hydrophobic spacers lead to rodlike micelles, in agreement with experiment.
b) As the bending stiffness of the hydrophobic spacer increases, so does the CMC.
c) Micelles with hydrophilic spacers are more or less spherical.
d) Bending stiffness in a hydrophilic spacer decreases the CMC.
e) The morphologies of ionic and nonionic geminis are identical regardless of whether the spacer is hydrophobic or hydrophilic. We are currently testing the "stiffness" predictions using acetylenic units in hydrophobic spacers and sugar units in hydrophilic spacers.

7. Surface Activity

The surface tension of water (72 mN m^{-1}) is typically reduced to 30–40 mN m^{-1} at the CMC of a surfactant. It is for this reason that surfactants are called "surface-active". Surface activity has a close connection to the wide-ranging applications of surfactants in virtually every major industry (pharmaceutical, food, metal, paint, petroleum, polymer, etc.). Perhaps this is a suitable time to take a pause from the laborious exposition of physical properties and to quote from a few abstracts of the many recent gemini patents. The objective here is to carry the reader (briefly, for we are academic types!) into the world of tangible reality:

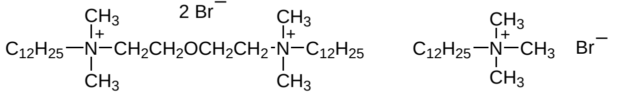
1) *Gemini-Type Betaine Surfactants from Amines and Aldehydes*: "Amphoteric amphiphilic compounds … are manufactured by condensation of C_6–C_{22} aldehydes with di-, oligo-, or polyamines, hydrogenation of the resulting condensation products, and carboxymethylation with $ClCH_2COOH$ or $ClCH_2COONa$. [The geminis] … can be combined with all current anionic, nonionic, cationic, and ampholytic surface-active agents and are particularly suitable for use as emulsifiers, antifoaming agents, detergents, dispersants, and hydrotropic agents in industry and in the home, e.g. in the metalworking field, in ore extraction, in the washing and cleaning of textiles, hard surfaces, the skin and the hair, and in cosmetics."[49]
2) *Gemini Polyhydroxy Fatty Acid Amide Surfactants for Detergents and Personal Care Compositions*: "Thus, D-glucose was reacted with 1,2-bis(3-aminopropoxy)ethane in the presence of Raney Ni to give a disugar diamine which was then amidated with methyl octanoate to give the gemini polyhydroxy fatty acid amide. The prepared gemini polyhydroxy fatty acid amide was suitable for use in dishwashing, detergents and laundry detergents (including fabric softening detergents)."[50]
3) *Manufacture of Novel Gemini Surfactants*: "The title surfactants, useful as wetting agents, oil-in-water emulsifiers and thickeners, are available through condensation of alk(en)yl oligoglucosides with bisepoxides."[51]
4) *Amphoteric Surfactants Having Multiple Hydrophobic and Hydrophilic Groups*: "The title amphoteric gemini surfactants, mild and environmentally benign, … are prepared."[52]
5) *Nonionic Gemini Surfactants and Their Blends*: "The title surfactants are extremely effective emulsifiers for oil-in-water emulsions that provide improved detergency at even low concentration levels."[53]

With this interlude behind us, we can now return to the question of surface activity. A favorite means of reporting surface activity is the c_{20} value representing the surfactant concentration that reduces the surface tension by an arbitrary 20 mN m^{-1}.[54] The c_{20} values reflect the tendency of surfactants to adsorb at the air/water interface. Specific numbers for an anionic gemini and its single-chained counterpart are given in Scheme 9.[6] It is seen that the gemini is three orders of



Scheme 9. The c_{20} values for an anionic gemini and its single-chained counterpart.

magnitude more surface-active. A comparison between a cationic gemini and conventional surfactant also shows a significant difference in surface activity (Scheme 10).[10, 35] A third example portraying the superiority of a gemini over an "ordinary" surfactant is shown in Scheme 11.[14]



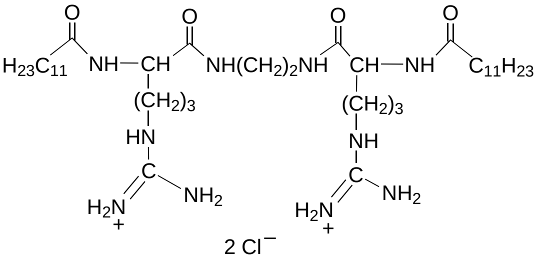
$C_{12}H_{25}-\overset{+}{N}(CH_3)_2-CH_2CH_2OCH_2CH_2-\overset{+}{N}(CH_3)_2-C_{12}H_{25}\quad 2\,Br^-$

$C_{12}H_{25}-\overset{+}{N}(CH_3)_2-CH_3\quad Br^-$

44 **45**

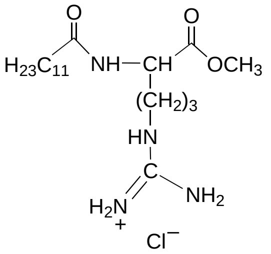
c_{20} = 0.25 mM c_{20} = 8 mM

Scheme 10. Comparison of the c_{20} values for a cationic gemini and a conventional surfactant.



8

c_{20} = 0.0003 mM



46

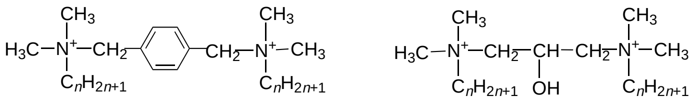
c_{20} = 0.6 mM

Scheme 11. Comparison of c_{20} values, showing the superiority of a gemini over an ordinary surfactant.

Why are geminis so prone to adsorb at the air/water interface? Rosen has ascribed the effect to a distortion of the water structure by the hydrophobic groups.[3] Accordingly, two hydrophobic groups in a single molecule are more disruptive than individual chains (with the hydrophilic groups contributing little to the change in water structure). Migration to the air/water interface of a micelle is thereby promoted. In our view, interfacial packing effects probably dominate any selective changes in water structure. There is evidence, in fact, that geminis do indeed form a more coherent interfacial film. This evidence is based upon the area-per-molecule for surfactants adsorbed at a saturated air/water interface as determined from surface tension data and the Gibbs adsorption equation.[31] A small cross-sectional area of the surfactant indicates a tight packing at the interface and an efficient lowering of the surface tension. Thus, a gemini surfactant bearing two sulfonate groups was shown to adsorb at the air/water interface with an area-per-chain of only 26 Å^2 compared to 43 Å^2 for a corresponding single-chained sulfonate.[55] Favorable packing was also found for bisquaternary ammonium geminis.[13] Apparently, the gemini spacer forces the pair of ionic groups to reside in a less space filling geometry relative to that of two ordinary surfactants. Of course, intermolecular distances between individual gemini molecules may not differ much from normal.

Mention should be made of a specialized but useful "maximum bubble pressure" method for monitoring dynamic surface tension, that is, the variation of surface tension with time.[56] (Adsorption of geminis at the air/water interface can sometimes be a slow process.[2]) In brief, the measurement is carried out by forcing known pressures of N_2 gas through a capillary into a surfactant solution to form bubbles. Pressure is converted into surface tension by using pure liquids of known surface tension as a calibration. Since data can be acquired in 10 ms, rather fast processes at the N_2/water interface can be observed. Typically, plots of dynamic surface tension versus time are divided into four stages: a) an induction period where there is little change; b) a region of rapid surface tension decrease; c) meso-equilibrium; and d) equilibrium regions.

Two geminis, one with a rigid, hydrophobic spacer and one with a flexible, more hydrophilic spacer (**47** and **48**, respectively), were examined by the maximum bubble pressure method.[57] It was found for all compounds that about two-thirds of the interface is covered at the end of the induction period just prior to the "fast-fall" region. In other words, there must be substantial surface coverage before an effect on the surface tension manifests itself. The time required to reach the fast-fall region depends heavily upon the chain length. In the aromatic series, for example, the C_{10} and C_{16} geminis have induction periods of about 0.2 and 10 s, respectively. Clearly, long chains inhibit diffusion-controlled organization into interfacial films. Induction times for geminis with a rigid spacer are shorter than for similar sized geminis with a flexible spacer. This is rather unexpected because one might have intuitively speculated that flexible geminis have greater diffusivity and, therefore, a smaller adsorption time. It may be that flexible spacers allow, for some reason, formation of cumbersome linear aggregates owing to chain–chain interactions. Viscosity data bear this out.[57]



47 **48**

8. Solubilization

Many organic compounds that are normally insoluble in water, or only slightly soluble, dissolve to a greater extent in the presence of micellar surfactant. The increased solubility (to form thermodynamically stable and isotropic solutions) is called "solubilization." Solubilization merits attention owing to its considerable technological relevance (detergency and tertiary oil recovery being only two examples of solubilization-dependant phenomena). Not surprisingly, the pioneers of surfactant chemistry were highly interested in solubilization. Thus, McBain and Richards found that potassium laurate micelles solubilized 0.23 moles of cyclohexane per mole of soap.[58] And Klevens reported that sodium dodecyl sulfate solubilized 0.87 moles of *n*-heptanol per mole of surfactant.[59]

A few aspects of solubilization, necessary to give the reader a feel for the subject, are compiled here:

a) The location within micelles of a solubilized compound (the "additive" component) depends upon its structure. Saturated hydrocarbons concentrate at the micellar core. A single functional group, however, shifts the additive's solubilization site to the interfacial region made up of the headgroups, the first few methylene groups of the chains, and water molecules.[60] Even nonpolar aromatic moieties prefer the interfacial region (especially with cationic micelles).
b) Generally speaking, an increase in surfactant chain length increases the solubilization power of the system.
c) Branching of the surfactant chain tends to diminish solubilization power.
d) For a given chain length, solubilization by micelles of different charge types usually follows the sequence nonionic > cationic > anionic.[61]
e) Introduction of a second ionic group to the polar end of a surfactant has been shown in one case to increase the solubilization of *n*-octanol, but to reduce the solubilization of *n*-octane.[51] This latter observation illustrates the complexity of the situation: multiple interactions take place within an aggregate whose variable structure is affected by a variety of parameters including the presence of an additive itself.

Solubilization in gemini micelles has not been examined in detail. The one exception (that we know of) involved the determination of the solubility of toluene and *n*-hexane in aqueous solutions of cationic geminis.[30] The experiments were carried out by shaking 3 mL of hydrocarbon with 30 mL of aqueous surfactant for many hours until clarity was achieved. Analysis of the water layer for hydrocarbon provided the solubilization power of the surfactant. It was found that, in the words of the authors, "the propensity of gemini micelles for oil solubilization is significantly better than of conventional surfactants; this is true on a molar basis as well as a weight basis".[30] For example, 12-2-12 gave a [toluene]/[surfactant] ratio of 3.8 compared to 0.78 for cetyltrimethylammonium bromide. The geminis showed a distinct preference for solubilizing toluene over *n*-hexane (owing, we presume, to ion–dipole interactions[62]). Thus, 10-2-10 and 12-2-12 led to [*n*-hexane]/[surfactant] ratios of only 0.29 and 0.99, respectively. (Inexplicably, *n*-hexane and 14-2-14 have a value which is at least ten times greater than that for cetyltrimethylammonium bromide.) It is proposed that the enhanced solubilization power of geminis may be related to tubular shapes of their aggregates discussed earlier in Section 6. In any event, the solubilization data bode well for future applications of geminis. Three useful applications that have already been published are given:

Geminis with a hydroxylated spacer (1,3-bis(dodecyl-*N*,*N*-dimethylammonium)-2-propanol dichloride (**4**, Scheme 1) and its C_{14} analogue) were used to separate all members of a family of 17 ergot alkaloids by micellar electrokinetic capillary chromatography.[63] Separation was achieved in less than 8 min using 20–40 mM surfactant in 50 mM phosphate buffer (pH 3.0) at 20°C. Corresponding single-chained surfactants (e.g. cetyltrimethylammonium bromide) failed to give complete separation of all components in the complex mixture. The precise mechanism of the difference is not understood.

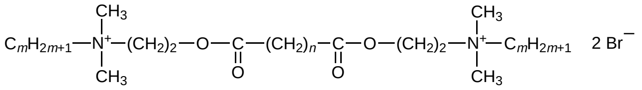
Polymerization of styrene into spherical and fairly monodisperse "latex" particles (10–100 nm in diameter depending upon conditions) can be carried out in oil-in-water microemulsions. Before delving into how geminis can play a role in the process, it is worthwhile to define "microemulsions". Oil-in-water microemulsions are thermodynamically stable, optically transparent mixtures of hydrocarbon and water in which tiny hydrocarbon droplets are dispersed in the water with the aid of (typically) a surfactant and a cosurfactant such as *n*-butanol or *n*-hexanol. It is amazing to watch 10% or more of hexane dissolve into water in the presence of a surfactant/cosurfactant combination. It turns out, however, that a few surfactants will form "ternary globular microemulsions" in styrene without the assistance of any cosurfactant. Among these are the *n*-alkyltrimethylammonium halides. By polymerizing styrene as "oil droplets" stabilized only by a cationic surfactant (conventional or gemini), one can avoid the complications of a fourth component. Further simplicity can be gained by using γ-ray irradiation, rather than a chemical initiator, to effect polymerization.[64] It was recognized that geminis are particularly interesting in such systems because surfactant shape, aggregation properties, and thus the interfacial spontaneous curvature can be easily "tuned" by changing the spacer length of the gemini. Spacer length contributes a new, easily adjustable structural parameter to the field of surfactant chemistry.

Geminis were found to be superior to conventional single-tailed surfactants in solubilizing styrene in water.[64] Among the 12-*n*-12 geminis ($n = 2, 4, 6, 8, 10, 12$), all formed single-phase oil-in-water microemulsions with styrene (although for $n = 2$ the stable microemulsion region in the phase diagram is very small). Latex particle size showed a modest dependence upon spacer length with a maximum at $n = 10$. For example, polymerization (at 25°C, surfactant-to-monomer ratio = 5, and 1,3-diisopropenylbenzene as a cross-linker) gave hydrodynamic radii ranging from 10 nm for $n = 2$ to 15 nm for $n = 10$. Weight-average molecular weights (at 25°C, surfactant-to-monomer weight ratio = 2, no cross-linker) varied from about 3×10^5 for $n = 2$ and $n = 12$ to 1.8×10^6 for $n = 6$. The data were attributed without details to different interfacial curvatures resulting from varying surfactant shapes. Uncertainties notwithstanding, the work serves to alert the colloid community to the tunability of properties of geminis in matters of practical importance.

While on the subject of practicality, mention should be made of the antimicrobial properties of geminis. Amphiphilic quaternary ammonium salts, such as benzyldodecyldimethylammonium bromide (BDDAB) and 2-ethoxycarbonylpentadecyltrimethylammonium bromide (EPTAB), are well-known disinfectants. The question was raised whether geminis of the general structure **49** (see Table 2) would display similar bioactivity.[65] In an amazingly thorough study, m was varied from 6 to 16, and n from 2 to 8, for a total of 45 compounds. Minimum inhibitory concentrations (MICs, defined as the lowest concentration of antibacterial agent inhibiting visible growth after 24 h incubation at 37 °C) were determined for this set of geminis against *E. coli* bacteria. By way of calibration, MICs for single-chained BDDAB and EPTAB were found to be 625 and 78 µM, respectively. Apparently the lower the MIC, the better.

Table 2 lists select MIC values for the gemini series.[65] The following generalizations emerge from the data: a) Short-chain compounds ($m = 6$) are not effective. b) Short spacers give lower MIC values. c) Lengthening the chain from $m = 12$ to $m = 16$ severely diminishes the activity; self-association effects in the compounds with $m = 16$ may be impairing interactions with the bacterial membranes. d) Optimal activity is achieved with $m = 10$ or 12. The gemini with $m = 12$ and $n = 2$ is one or two orders of magnitude more potent than the conventional single-chained disinfectants BDDAB and EPTAB. Surpassing the commercial compounds to this degree is a noteworthy achievement. One wonders about the bioactivity of the other classes of geminis, not only as disinfectants but as anti-viral agents and mediators of transfection.

Table 2. Minimum inhibitory concentrations (MICs) against *E. coli* for gemini surfactants **49**.



$$C_mH_{2m+1}-N^+(CH_3)_2-(CH_2)_2-O-C(=O)-(CH_2)_n-C(=O)-O-(CH_2)_2-N^+(CH_3)_2-C_mH_{2m+1}\quad 2\,Br^-$$

49

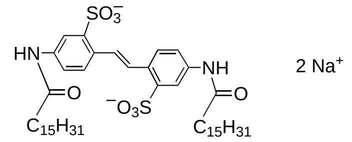
Gemini[a]		MIC [µM]
m	n	
6	2	21000
12	2	6
16	2	5700
6	4	8100
12	4	25
16	4	2800
6	8	930
12	8	190
16	8	5200

[a] m = chain length, n = spacer length.

9. Gemini Films

In Section 7 on surface activity, we alluded to the fact that water-soluble surfactants adsorb at the air/water interface and, in this manner, lower the surface tension. Water-insoluble amphiphiles, on the other hand, can often be spread onto a water surface in the form of a film only one molecule thick (an "insoluble monolayer"). With the aid of a device called a film balance, a monolayer can be compressed with a moveable barrier while, simultaneously, recording the pressure generated by the film. If, for example, the film component is in a "gaseous" state, there will be little pressure change as the film is compressed. If the film molecules are highly compacted, then the pressure will rise steeply as the film is further compressed. Considerable information on the orientation and packing behavior of molecules at the air/water interface can thus be obtained by plotting surface pressure versus film area-per-molecule to give pressure-area ($\pi - A$) isotherms. This section is devoted to monolayer films of two gemini systems.

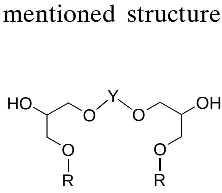
A gemini of interest, **50**, has two sulfonates attached directly to a photoactive stilbene spacer.[12] The compound can be spread as a stable monolayer by depositing a solution in chloroform onto pure water and allowing the chloroform to evaporate. The $\pi - A$ isotherm showed a steep rise in surface pressure at around 140 Å^2 per molecule, indicating a close packing at this area. Further compression caused the film to buckle and collapse. Now the area of 140 Å^2 is much larger than the areas of the two chains (40 Å^2). The area of 140 Å^2 reflects, therefore, the stilbene spacer lying parallel to the surface of the water with the sulfonate groups immersed in the water and the hydrophobic tails extended into the air. Upon irradiation of the film at 366 nm, the $\pi - A$ isotherm changed drastically. Most notably, there ensued a large decrease in the surface area at constant pressure. This is consistent with a *trans*-to-*cis* isomerization of the stilbene, a conclusion supported by spectral properties of the film after being transferred to a quartz plate. Irradiation of the *cis* monolayer at 254 nm led to an increase in surface area as the *trans* isomer was regenerated.



50

The efficient *trans*-to-*cis* conversion was puzzling because the reaction was known to be strongly inhibited in condensed monolayers that resist extensive molecular reorganization. Fluorescence microscopy helped explain the unusual facility of the isomerization. Thus, *trans*-gemini was mixed with 2% of a fluorescent dye prior to deposition upon the water. Upon compression of the film, dark nonfluorescent domains, representing regions of crystalline gemini that had "squeezed out" the dye, were evident under the fluorescence microscope. When the film was irradiated at 366 nm, the domains disappeared and the entire microscope field took on a uniform fluorescence. It was concluded that initially formed *cis* isomer provided a fluid medium in which *trans* gemini is sufficiently mobile to further isomerize. In the absence of such a photoinduced solid-to-fluid transition, reversible photoisomerization would have been difficult to achieve.

A second article dealing with pressure–area isotherms of gemini-type structures begins with the following sentence: "Because almost all the surfactants in general use consist simply of one hydrophobic alkyl chain and one hydrophilic headgroup, there are limitations to modifying or improving the surface-active properties within the range of the above-mentioned structure."[66] We heartily agree with the sentiment; geminis have added a new dimension to surfactant chemistry. In the paper just quoted, the focus is on the monolayer properties of compounds **51** ($R = C_{10}H_{21} - C_{18}H_{37}$, $Y = C_2H_4 - C_6H_{12}$). In this particular study, the free hydroxy groups were not further derivatized to sulfates or other ionic groups because monolayer formation requires compounds that are reasonably insoluble in water. Figure 2 shows how films with $R = C_{10}H_{21}$ expand as the spacer is lengthened from $Y = C_2H_4$ to $Y = C_4H_8$ and $Y = C_6H_{12}$ (a, b, and c, respectively). Monolayers packed more tightly as the chain length R was increased. This was seen, for example, from "liftoff areas" defined as the first point on the $\pi - A$ isotherm showing a detectable resistance to compression by the moveable barrier. Since the liftoff area for $R = C_{10}H_{21}/Y = C_6H_{12}$ is 239 Å^2, compared to only 138 Å^2 for $R = C_{18}H_{37}/Y = C_6H_{12}$, the latter has a greater propensity to assemble into a condensed monolayer owing, no doubt, to favorable alignment of the chains. Limiting area, defined as the molecular area at zero pressure (obtained by extrapolation) showed the same thing. Limiting areas for $R = C_{10}H_{21}/Y = C_6H_{12}$ and $R = C_{18}H_{37}/Y = C_6H_{12}$ were found to be 174 and 130 Å^2 per molecule, respectively.



51

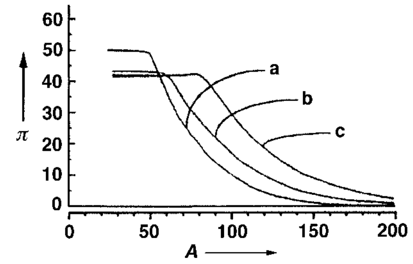


Figure 2. Effect of spacer length on pressure–area isotherms for 10-O-*n*-O-10 geminis where $n = 2$ (a), 4 (b), and 6 (c). Pressure π is in mN m^{-1} and area A in Å^2 per molecule. Taken from ref. [66].

The films studied in the above work can be contrasted with soluble films composed of simple 12-*n*-12 cationic geminis as examined experimentally[31] and theoretically.[67] It turns out that the area-per-surfactant molecule at the air/water interface (determined from surface tension data and the Gibbs equation) increases rapidly for short spacers, reaches a maximum at 10–12 methylene groups, and decreases with even longer spacers (Figure 3).[31] The nonmonotonic dependence of molecular area on the spacer length is accounted for theoretically by the interplay of three factors: a) a simple geometrical effect in which area expands as does the spacer; b) a gemini–gemini interaction that tends to decrease the specific area beyond a certain spacer length; and c) an entropic effect of flexible spacers that accentuates the second factor.[67] In our opinion, "hair-pin turns" among sufficiently long spacers could impart areas that are smaller than expected and, therefore, account for the right-hand wing of the bell-shaped curve. According to the calculations, however, spacers do not depart from the air/water interface.[67] If this is true, then our looping conformers would have to reside on the water surface. In connection with conformational issues, attention is drawn to selective decoupling ^{13}C and ^1H NMR studies which address the subject in detail.[68]

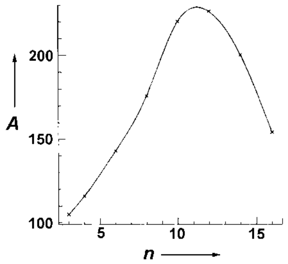


Figure 3. Plot of area A [Å^2] per surfactant molecule at the air/water interface against spacer length n for 12-*n*-12. Taken from ref. [67].

10. New Materials

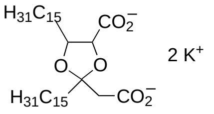
Introducing pores of controlled size and shape into silica and other common materials offers great opportunities to those interested in topics such as shape-selective catalysis, molecular sieving, chemical sensing, and selective adsorption.[69] The fashioning of porous silica received a great impetus less than ten years ago when cationic surfactants were first used in the conversion of silicate anions into mesoporous molecular sieves.[70] Presumably, polyanionic oligomeric silicate can ion-exchange with surfactant counterions (often bromide). Intermicellar repulsion is thereby reduced, and the resulting aggregates provide a template for the ensuing silica mesophase formation. One of the most promising materials made in this manner, called MCM-48, is cubic in structure and is characterized by a three-dimensional pore system. Since conventional alkyltrimethylammonium surfactants give hexagonal or lamellar structures rather than high-quality MCM-48, a search began for alternative surfactants.[71] Cationic geminis, particularly those with long spacers such as 16-12-16 and 18-12-18, have been shown to promote the synthesis of excellent quality MCM-48 with high surface area and narrow pore-size distribution.[72, 73] However, in order to help place things in proper context, it will be useful to first give directions for making MCM-48.[69]

Gemini surfactant is dissolved in basic water and then mixed with $Si(OEt)_4$ in a ratio of gemini/NaOH/H_2O/$Si(OEt)_4$ of 0.06/0.6/150/1. The mixture is stirred for 2 h at room temperature and then placed in an autoclave at 100 °C for several days. The resulting white solid is removed by vacuum filtration, added to fresh water (20 g per one g solid), and autoclaved at 100 °C once again. In the final step, the solid precursor is heated in ambient air ("calcined") from room temperature to 550 °C at a heating rate of 5 deg min^{-1}. With this procedure, production of high-quality MCM materials has been reduced from several weeks to a few days. Making MCM-48 is simplicity itself.[69]

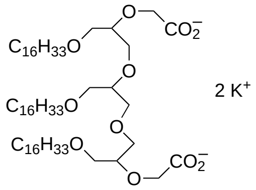
Both geminis 18-12-18 and 16-12-16 yield excellent MCM-48 with a surface area of 1200–1600 $m^2 g^{-1}$ and pore volumes exceeding 1.2 mL g^{-1}.[69] Narrow pore-size distributions are obtained for MCM-48 with pore radii of 12 and 13 Å when using 16-2-16 and 18-2-18, respectively. The spacer length of the gemini surfactant determines the crystallographic phase that is formed, whereas the chain length determines the average pore size. VO_x has been grafted onto gemini-based MCM-48, demonstrating the potential of the material in heterogeneous catalysis.[73] Gemini surfactants clearly have a promising future in materials technology.

11. Vesicles, Gels, and Phase Behavior

We end this review by citing, briefly in each case, examples of gemini surfactants that self-assemble into interesting structures. Compound **52** was called a "double-chain, double-head group surfactant" (an accurate but lengthy description of a gemini, making us glad we coined the euphemism)[1, 2] that forms vesicles when sonicated in aqueous base.[74] At pH 9.2, the vesicles have hydrodynamic diameters of about 360 Å. Stable vesicles, in which entrapped guests remain for months, can be made from triple-chained gemini **53**.[75] Encapsulation is one of many potential applications of geminis that remain to be exploited.



52

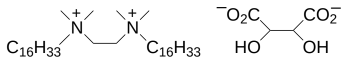


53

Diastereomeric gemini surfactants **32** (Scheme 6), bearing two phosphate groups, form unilamellar vesicles upon sonication (150–250 Å for *S*,*S* and 500–1000 Å for *R*,*S*).[76] Remarkably, when Ca^{2+} is added to the vesicles, the *S*,*S* isomer undergoes fusion, whereas the *R*,*S* isomer undergoes fission. The difference is attributed to a Ca^{2+} effect on headsize which increases with the *S*,*S* isomer but decreases with the *R*,*S* isomer.

A solution of 5% (w/w) 12-2-12 in water is viscous, a fact consistent with wormlike micelles. When *n*-hexanol is added, it is possible to induce a micelle-to-vesicle transition.[77, 78] Viscosity data, coupled to cryo-transmission electron microscopy, reveal the details of the process. Thus, at lower levels of *n*-hexanol the viscosity increases as the small OH headgroups of the alcohol decrease the spontaneous curvature of the micelles (i.e., flatten the interface) and thereby elongate the micelles. The viscosity ultimately decreases rapidly at higher *n*-hexanol concentrations; this is attributed to a spontaneous curvature close to zero where relatively flat vesicles and highly branched micelles are favored. At even greater *n*-hexanol concentrations, the vesicles assume microscopically visible tubulelike shapes hundreds of microns long.

Gemini surfactants composed of 16-2-16 with L- and D-tartrate counterions (**54**) have been reported to gelate organic solvents (CH_2Cl_2, $CHCl_3$, toluene, etc.) containing traces of water.[79] As little as 10 mM gemini can immobilize the solvent. Transmission electron microscopy reveals the presence of long, entangled helical fibers (right handed for L-tartrate, and left-handed for D-tartrate counterions). A proposed structure of the gel is shown in Figure 4, but other modes of bridging the cationic layers cannot be excluded. Layerlike liquid crystalline phases of "counterion-coupled gemini surfactants" or "cocogems" have been used as media for polymerizing acrylamide.[80] The overall morphology of the resulting polymer gel is controlled by the anisotropy of the surfactant assembly.



54

Phase behavior is an important property of surfactants, assembling as they do into "lyotropic liquid crystalline mesophases" when mixed with water and into "thermotropic liquid crystalline phases" when heated. Discussions of the subject often refer to characteristic textures, to phase diagrams, and to mesophases such as H_1, V_1, L_α, and L_β. Polarized optical microscopy, calorimetry, X-ray diffraction, neutron scattering, and viscometry are favorite tools in the exploration of phase behavior. Clearly, the topic is too esoteric for the general reader. Suffice it to say here that geminis have a unique phase behavior and that those interested in learning more can consult the literature.[81–84]

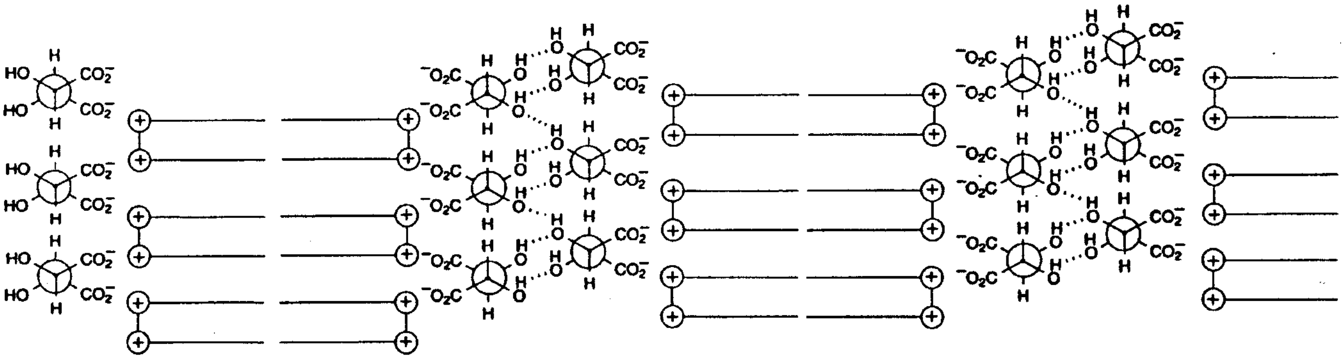


Figure 4. Proposed structure of aggregates of a gemini with tartrate counterions. Taken from ref. [79].

12. Concluding Remarks

Writing a review is something like preparing a buffet dinner. Multiple dishes are set forth, and the hungry can select or not select; consume as presented or enhance with spices and sauces; come back for more or resist the temptation. With both buffets and reviews, the hope is that the participant ends up reasonably content. There is, however, a philosophic difference between buffets and reviews. In a buffet, the diner will rather quickly become sated and ready to leave. With a well-written review, at least a few readers might want to continue on, perhaps for many years. In the case at hand, this could involve the synthesis of new members of the gemini family (an intense interest of ours); or the development of new gemini-based materials; or the application of geminis to skin care and transdermal drug delivery; or the use of chiral geminis for separating enantiomers chromatographically; or the fabrication of new transfection agents. Indeed, geminis could well turn out to be more useful to the person in the street than (for example) crown ethers and fullerenes.[85]

We wish to express our appreciation to the National Institutes of Health, the Army Research Office, and the National Science Foundation for supporting this work.

Received: April 21, 1999 [A339]

---

[1] F. M. Menger, C. A. Littau, *J. Am. Chem. Soc.* **1991**, *113*, 1451–1452.

[2] F. M. Menger, C. A. Littau, *J. Am. Chem. Soc.* **1993**, *115*, 10083–10090.

[3] M. J. Rosen, *CHEMTECH* **1993**, *23*, 30–33.

[4] C. A. Bunton, L. Robinson, J. Schaak, M. F. Stern, *J. Org. Chem.* **1971**, *36*, 2346–2350.

[5] F. Devínsky, L. Masárová, I. Lacko, *J. Colloid Interface Sci.* **1985**, *105*, 235–239.

[6] Y.-P. Zhu, A. Masuyama, M. Okahara *J. Am. Oil Chem. Soc.* **1990**, *67*, 459–463.

[7] M. J. Rosen, D. J. Tracy, *J. Surfactants Deterg.* **1998**, *1*, 547–554.

[8] R. Zana, M. Benrroau, R. Rueff, *Langmuir* **1991**, *7*, 1072–1075.

[9] S. De, V. K. Aswal, P. S. Goyal, S. Bhattacharya, *J. Phys. Chem. B* **1998**, *102*, 6152–6160.

[10] T.-S. Kim, T. Kida, Y. Nakatsuji, T. Hirao, I. Ikeda, *J. Am. Oil Chem. Soc.* **1996**, *73*, 907–911.

[11] Y.-P. Zhu, A. Masuyama, Y. Kobata, Y. Nakatsuji, M. Okahara, M. J. Rosen, *J. Colloid Interface Sci.* **1993**, *158*, 40–45.

[12] O. Karthaus, M. Shimomura, *J. Am. Chem. Soc.* **1996**, *118*, 9174–9175.

[13] M. Diaz, A. Manresa, A. Pinazo, P. Erra, M. R. Infante, *J. Chem. Soc. Perkin Trans. 2* **1994**, 1871–1876.

[14] L. Pérez, A. Pinazo, M. J. Rosen, M. R. Infante, *Langmuir* **1998**, *14*, 2307–2315.

[15] P. Renouf, C. Mioskowski, L. Lebeau, D. Hebrault, J.-R. Desmurs, *Tetrahedron Lett.* **1998**, *39*, 1357–1360.

[16] R. Zana, *Colloids Surf. A* **1997**, *123–124*, 27–35.

[17] F. M. Menger, V. A. Migulin, unpublished results.

[18] M. J. L. Castro, J. Kovensky, A. F. Cirelli, *Tetrahedron Lett.* **1997**, *38*, 3995–3998.

[19] R. Oda, I. Huc, S. J. Candau, *Chem Commun.* **1997**, 2105–2106.

[20] R. Zana, H. Levy, D. Papoutsi, G. Beinert, *Langmuir* **1995**, *11*, 3694–3698.

[21] M. J. Rosen, T. Gao, Y. Nakatsuji, A. Masuyama, *Colloids Surf. A* **1994**, *88*, 1–11.

[22] K. Esumi, M. Goino, Y. Koide, *J. Colloid Interface Sci.* **1996**, *183*, 539–545.

[23] We have synthesized a series of dendrimeric surfactants with as many as 20 tails. F. M. Menger, A. V. Peresypkin, unpublished results.

[24] F. L. Duivenvoorde, M. C. Feiters, S. J. van der Goost, J. B. F. N. Engberts, *Langmuir* **1997**, *13*, 3737–3743.

[25] N. A. J. M. Sommerdijk, T. H. L. Hoeks, M. Synak, M. C. Feiters, R. J. M. Nolte, B. Zwanenburg, *J. Am. Chem. Soc.* **1997**, *119*, 4338–4344.

[26] Y.-P. Zhu, A. Masuyama, Y. Kirito, M. Okahata, *J. Am. Oil Chem. Soc.* **1991**, *68*, 539–543.

[27] K. Jennings, I. Marshall, H. Birrell, A. Edwards, N. Haskins, O. Soderman, A. J. Kirby, P. Camilleri, *Chem. Commun.* **1998**, 1951–1952.

[28] F. M. Menger, R. Zana, B. Lindman, *J. Chem. Ed.* **1998**, *75*, 115.

[29] L. D. Song, M. J. Rosen, *Langmuir* **1996**, *12*, 1149–1153.

[30] T. Dam, J. B. F. N. Engberts, J. Karthäuser, S. Karaborni, N. M. van Os, *Colloids Surf. A* **1996**, *118*, 41–49.

[31] E. Alami, G. Beinert, P. Marie, R. Zana, *Langmuir* **1993**, *9*, 1465–1467.

[32] J. Zhao, S. D. Christian, B. M. Fung, *J. Phys. Chem. B* **1998**, *102*, 7613–7618.

[33] M. Frindi, B. Michels, H. Levy, R. Zana, *Langmuir* **1994**, *10*, 1140–1145.

[34] F. Devínsky, I. Lacko, F. Bitterová, L. Tomecková, *J. Colloid Interface Sci.* **1986**, *114*, 314–322.

[35] M. J. Rosen, L. Liu, *J. Am. Oil Chem. Soc.* **1996**, *73*, 885–890.

[36] T.-S. Kim, T. Kida, Y. Nakatsuji, I. Ikeda, *Langmuir* **1996**, *12*, 6304–6408.

[37] Y.-P. Zhu, A. Masuyama, M. Okahara *J. Am. Oil Chem. Soc.* **1990**, *67*, 459–463.

[38] A. L. Underwood, E. W. Anacker, *J. Colloid Interface Sci.* **1984**, *100*, 128–135.

[39] R. G. Alargova, I. I. Kochijashky, M. L. Sierra, R. Zana, *Langmuir* **1998**, *14*, 5412–5418.

[40] H. Hirata, N, Hattori, M. Ishida, H. Okabayashi, M. Frusaka, R. Zana, *J. Phys. Chem.* **1995**, *99*, 17778–17784.

[41] V. K. Aswal, S. De, P. S. Goyal, S. Bhattacharya, R. K. Heenan, *Phys. Rev. E* **1998**, *57*, 776–783.

[42] S. De, V. K. Aswal, P. S. Goyal, S. Bhattacharya, *J. Phys. Chem.* **1996**, *100*, 11664–11671.

[43] F. Reiss-Husson, V. Luzzati, *J. Phys. Chem.* **1964**, *68*, 3504–3511.

[44] V. K. Aswal, S. De, P. S. Goyal, S. Bhattacharya, R. K. Heenan, *J. Chem. Soc. Faraday Trans.* **1998**, *94*, 2965–2967.

[45] D. Danino, Y. Talmon, R. Zana, *Langmuir* **1995**, 11, 1448–1456.

[46] V. Scmitt, F. Schosseler, F. Lequeux, *Europhys. Lett.* **1995**, *30*, 31–36.

[47] R. Oda, P. Panizza, M. Schmutz, F. Lequeux, *Langmuir* **1997**, *13*, 6407–6412.

[48] P. K. Maiti, D. Chowdhury, *J. Chem. Phys.* **1998**, 109, 5126–5133.

[49] K. Kwetkat (Hüls AG), WO-B 9731890, **1997** [*Chem. Abstr.* **1997**, *127*, 249754r].

[50] J. J. Scheibel, D. S. Conner, Y. C. Fu (Proctor and Gamble Co.), US-A 5534197, **1996** [*Chem. Abstr.* **1996**, *125*, 171553m].

[51] O. Rhode, H.-C. Raths (Henkel K.G. a.A.), DE-B 19645189, **1998** [*Chem. Abstr.* **1998**, *128*, 323164n].

[52] D. J. Tracy, R. Li, J. Yang (Rhodia Inc.), US-A 5789371, **1998** [*Chem. Abstr.* **1998**, *129*, 177210b].

[53] D. J. Tracy, R. Li (Rhone-Poulenc Inc.), WO-B 9823365, **1998** [*Chem. Abstr.* **1998**, *129*, 55770p].

[54] M. J. Rosen, *Surfactants and Interfacial Phenomena*, 2nd ed., Wiley, New York, **1989**, chap. 2, 3, 5.

[55] Y.-P. Zhu, A. Masuyama, T. Nagata, M. Okahara, *Yukagaku* **1991**, *40*, 473–477.

[56] X. Y. Hua, M. J. Rosen, *J. Colloid Inteface Sci.* **1988**, *124*, 652–659.

[57] M. J. Rosen, L. D. Song, *J. Colloid Interface Sci.* **1996**, *179*, 261–268.

[58] J. W. McBain, P. H. Richards, *Ind. Eng. Chem.* **1946**, *38*, 642–646.

[59] H. B. Klevens, *Chem. Rev.* **1950**, *47*, 1–74.

[60] D. Myers, *Surfactants Science and Technology*, VCH, New York, **1988**, pp. 156–158.

[61] S. Saito, *J. Colloid Interface Sci.* **1967**, *24*, 227–234.

[62] S. Mecozzi, A. P. West, Jr., D. A. Dougherty, *J. Am. Chem. Soc.* **1996**, *118*, 2307–2308.

[63] K. Chen, D. C. Locke, T. Maldacker, J.-L. Lin, S. Aawasiripong, U. Schurrath, *J. Chromatogr. A* **1998**, *822*, 281–290.

[64] M. Dreja, B. Tieke, *Langmuir* **1998**, *14*, 800 – 807.
[65] M. Pavlíková, I. Lacko, F. Devínský, D. Mlynarèík, *Collect. Czech. Chem. Commun.* **1995**, *60*, 1213 – 1228.
[66] Y. Sumida, A. Masuyama, T. Oki, T. Kida, Y. Nakatsuji, I. Ikeda, M. Nojima, *Langmuir* **1996**, *12*, 3986 – 3990.
[67] H. Diamant, D. Andelman, *Langmuir* **1994**, *10*, 2910 – 2916.
[68] N. Hattori, A. Yoshino, H. Okabayoshi, C. J. O'Conner, *J. Phys. Chem. B* **1998**, *102*, 8965 – 8973.
[69] P. Van Der Voort, M. Mathieu, F. Mees, E. F. Vansant, *J. Phys. Chem. B* **1998**, *102*, 8847 – 8851.
[70] C. T. Kresge, M. E. Leonowicz, W. J. Roth, J. C. Vartuli, J. S. Beck, *Nature* **1992**, *359*, 710 – 712.
[71] Q. Huo, D. I. Margolese, G. D. Stucky, *Chem. Mater.* **1996**, *8*, 1147 – 1160.
[72] S. Manne, T. E. Schäffer, Q. Huo, P. K. Hansma, D. E. Morse, G. D. Stucky, I. A. Askay, *Langmuir* **1997**, *13*, 6382 – 6387.
[73] P. Van Der Voort, M. Morey, G. D. Stucky, M. Mathieu, E. F. Vansant, *J. Phys. Chem. B* **1998**,*102*, 585 – 590.
[74] D. J. Jaeger, E. L. G. Brown, *Langmuir* **1996**, *12*, 1976 – 1980.
[75] Y. Sumida, A. Masuyama, H. Maekawa, M. Takasu, T. Kida, Y. Nakatsuji, I. Ikeda, M. Nojima, *Chem. Commun.* **1998**, 2385 – 2386.
[76] N. A. J. M. Sommerdijk, T. H. L. Hoeks, M. Synak, M. C. Feiters, R. J. M. Nolte, B. Zwanenburg, *J. Am. Chem. Soc.* **1997**, *119*, 4338 – 4344.
[77] R. Oda, L. Bourdieu, M. Schmutz, *J. Phys. Chem. B* **1997**, *101*, 5913 – 5916.
[78] R. Oda, I. Huc, S. J. Candau, *Chem. Commun.* **1997**, 2105 – 2106.
[79] R. Oda, I. Huc, S. J. Candau, *Angew. Chem.* **1998**, *110*, 2835 – 2838; *Angew. Chem. Int. Ed.* **1998**, *37*, 2689 – 2691.
[80] M. Antonietti, C. Göltner, H.-P. Hentze, *Langmuir* **1998**, *14*, 2670 – 2676.
[81] K. M. Layn, P. G. Debenedetti, R. K. Prud'homme, *J. Chem. Phys.* **1998**, *109*, 5651 – 5658.
[82] E. Buhler, E. Mendes, P. Boltenhagen, J. P. Munch, R. Zana, S. J. Candau, *Langmuir* **1997**, *13*, 3096 – 3102.
[83] S. Fuller, N. N. Shinde, G. J. T. Tiddy, *Langmuir* **1996**, *12*, 1117 – 1123.
[84] M. Dreja, S. Gramberg, B. Tieke, *Chem. Commun.* **1998**, 1371 – 1372.
[85] Recent work from our own group on gemini surfactants not mentioned in this review includes: F. M. Menger, V. A. Migulin, *J. Org. Chem.* **1999**, *64*, 8916 – 8921; A. V. Peresypkin, F. M. Menger, *Org. Lett.* **1999**, *1*, 1347 – 1350; F. M. Menger, J. S. Keiper, V. Azov, *Langmuir* **2000**, *16*, 2062 – 2067.