A Search for a Relation between Aggregate Morphology and the Structure of 1,4-Dialkylpyridinium Halide Surfactants

Jan Jaap H. Nusselder and Jan B. F. N. Engberts*

Department of Organic Chemistry, University of Groningen, Nijenborgh 16, 9747 AG Groningen, The Netherlands

Received March 12, 1991

A detailed study of the relation between the aggregate morphology and the molecular shape of 27 1-alkyl-4-(or 2-)alkyl(or *n*-alkoxycarbonyl)pyridinium halide surfactants is described. This shape can be expressed in a molecular packing parameter (*P*) as suggested by Israelachvili. For unbranched 1-methyl-4-*n*-alkylpyridinium iodides, the packing parameter does not depend on the length of the alkyl chain (n_c). Spherical micelles formed from these surfactants grow into rodlike micelles. The critical rod concentration (crc) is, however, dependent on n_c. This originates from the dependence of the aggregation number of spherical micelles on n_c, in agreement with predictions based on the ladder model. Alkyl chain branching in 1-methyl-4-(C_{12}-alkyl)pyridinium iodides affects the shape of the surfactant. Branching near the headgroup decreases *P* and dramatically lessens the propensity of the spherical micelle to grow. Branching near the chain end increases *P* and decreases the crc. Highly branched surfactant monomers associate into bilayers, which can be transformed into vesicles. The overall results indicate that the morphology of the aggregate is mainly dependent on the shape of the surfactant. The possibility for backfolding of the 1-alkyl chain of 1-alkyl-4-*n*-dodecylpyridinium iodide surfactants directly affects the preferred morphology of the aggregate. Bilayers are formed if backfolding occurs; otherwise spherical micelles are formed, which, on increasing surfactant concentration, grow into rodlike micelles. Interestingly, 1-methyl-4-(*n*-alkoxycarbonyl)pyridinium iodides associate into bilayers, independent of the length of the alkyl chain (n_c = 10–16). This aggregation behavior probably stems from a special kind of interdigitation, which changes the geometrical constraints for packing into a bilayer.

Introduction

Association of surfactant monomers in water may lead to the formation of a variety of aggregates like spherical micelles, rodlike (threadlike) micelles, or bilayer membranes, depending on the precise molecular structure of the surfactant molecule. Furthermore, factors such as temperature, surfactant concentration, cosolvent, added electrolytes, and nature of the counterion play a role. A nice illustration of the effect of changes in surfactant structure on aggregate stability is provided by the different aggregation behavior of a series of short-chain (a)symmetric 1,2-diacyl-*sn*-glycero-3-phosphocholines (C_nC_mPC). Di-C_6-PC forms spherical micelles that do not grow significantly upon increasing the surfactant concentration.[1] However, if in one of the two acyl chains one additional methylene group is present, the spherical micelles grow appreciably when the surfactant concentration is increased.[1b,2] For di-C_8-PC just above the cmc, a phase transition, presumably into a lamellar phase, is observed.[3] *n*-Dodecylalkyldimethylammonium bromide surfactants also form spherical micelles, disk- or rodlike micelles, or vesicles, depending on the number of carbon atoms in the second alkyl chain.[4] Recently, the so-called catanionic surfactants, which combine oppositely charged surfactants, have also been employed in studies aimed at establishing a dependence of the aggregate morphology on surfactant structure.[5]

In the preceding examples, the changes in the structure of the surfactant influenced both the shape and the hydrophobicity of the molecule. In a preliminary study, we have investigated a series of *isomeric* 1-methyl-4-(C_{12}-alkyl)pyridinium iodides in which the structure of the C_{12}-alkyl chain was only altered by chain branching.[6] In this approach, the hydrophobic effect, which constitutes the driving force for aggregation, remains almost invariant. Interestingly, under these conditions chain branching dramatically affects the preference for a certain aggregate morphology. It appears that the entire range of spherical micelles, rodlike micelles and vesicles, can be formed from these *isomeric* surfactants. In contrast, the *properties* of spherical micelles are scarcely influenced by the shape of the surfactant, apart from the packing of the alkyl chains.[7-9]

Israelachvili and co-workers[10] have defined a packing parameter, *P* (eq 1), which is related to the shape of a

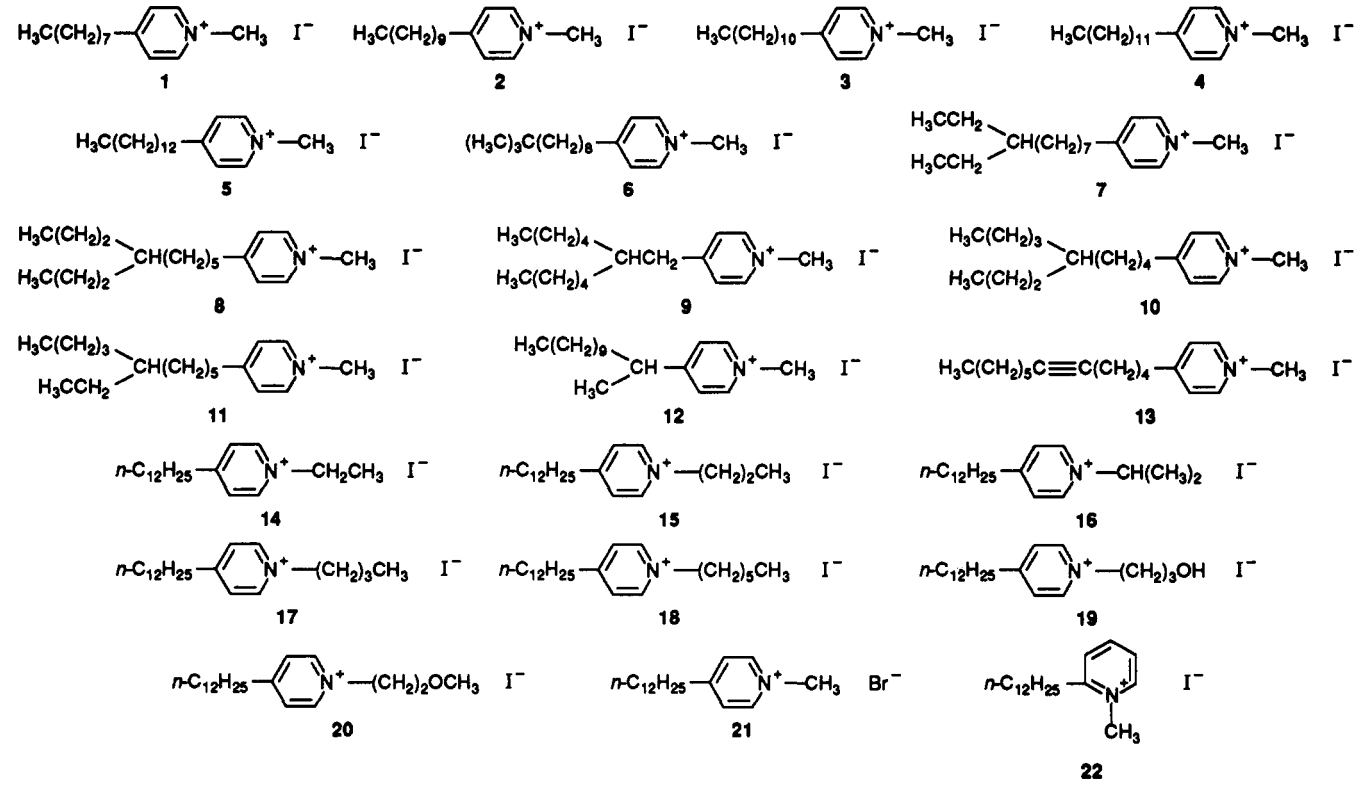
$$P = v/(a_o \cdot l_c) \quad (1)$$

surfactant molecule. Herein, v is the volume of the hydrocarbon chain, a_o the optimal surface area per headgroup in the aggregate, and l_c the length of the alkyl chain. These authors have defined a theoretical relation between this parameter and the morphology of an aggregate. However, surprisingly few experimental studies have been described in the literature that deal with this relation. Therefore we present herein a detailed study of the aggregation of 1-alkyl-4-(or 2-)alkylpyridinium halide surfactants in an endeavor to find a relation between the thermodynamic stability of the various aggregates and the structure of the surfactant molecule. The following structural features have been varied: (i) the length of the 4-alkyl group in a series of 1-methyl-4-alkylpyridinium iodide surfactants, **1–5**; (ii)

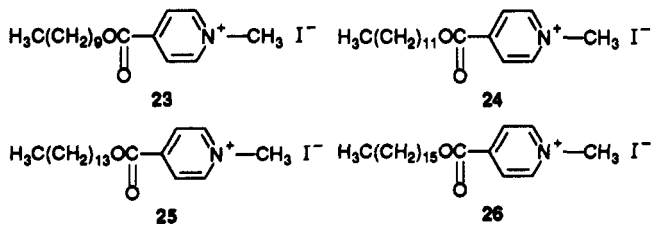
(1) (a) Tausk, R. J. M.; van Esch, J.; Karmiggelt, J.; Voordouw, G.; Overbeek, J. T. G. *Biophys. Chem.* **1974**, *1*, 184. (b) Lin, T.-L.; Chen, S.-H.; Gabriël, N. E.; Roberts, M. F. *J. Am. Chem. Soc.* **1986**, *108*, 3499.
(2) (a) Lin, T.-L.; Chen, S.-H.; Roberts, M. F. *J. Am. Chem. Soc.* **1987**, *109*, 2321. (b) Lin, T.-L.; Chen, S.-H.; Gabriël, N. E.; Roberts, M. F. *J. Phys. Chem.* **1987**, *91*, 406.
(3) Tausk, R. J. M.; Oudshoorn, C.; Overbeek, J. T. G. *Biophys. Chem.* **1974**, *2*, 53.
(4) (a) Lianos, P.; Lang, J.; Zana, R. *J. Colloid Interface Sci.* **1983**, *91*, 276. (b) Verrall, R. E.; Milioto, S.; Zana, R. *J. Phys. Chem.* **1988**, *92*, 3939.
(5) Yu, Z.-J.; Zhou, Z.; Xu, G. *J. Phys. Chem.* **1989**, *93*, 7446.
(6) Nusselder, J. J. H.; Engberts, J. B. F. N. *J. Am. Chem. Soc.* **1989**, *111*, 5000.
(7) Nusselder, J. J. H.; de Groot, T.-J.; Trimbos, M.; Engberts, J. B. F. N. *J. Org. Chem.* **1988**, *53*, 2423.
(8) Nusselder, J. J. H.; Engberts, J. B. F. N. *J. Phys. Chem.* **1989**, *93*, 6142.
(9) Nusselder, J. J. H.; Engberts, J. B. F. N. Submitted for publication.
(10) (a) Israelachvili, J. N.; Mitchel, D. J.; Ninham, B. W. *J. Chem. Soc., Faraday Trans. II* **1976**, *72*, 1525. (b) Israelachvili, J. N. In *Physics of Amphiphiles: Micelles, Vesicles and Microemulsions*; Degorgio, V., Corti, M., Eds.; North-Holland: Amsterdam, 1985; p 4.

0022-3263/91/1956-5522$02.50/0

Chart I



the degree of branching of the 4-alkyl group in 1-methyl-4-(C_{12}-alkyl)pyridinium iodides **4** and **6–12**; (iii) the stiffness of the 4-alkyl group in **4** and **13**; (iv) the counterion type in 1-methyl-4-*n*-dodecylpyridinium halides **4** and **21**; (v) the substitution pattern of the pyridinium ring in **4** and **22**; and (vi) the hydrophobicity of the 1-alkyl group in a series of 1-alkyl-4-*n*-dodecylpyridinium iodide surfactants **4** and **14–20** (Chart I). The rather unexpected aggregation behavior of a series of 1-methyl-4-(*n*-alkoxycarbonyl)pyridinium iodides (**23–26**) will be discussed as well. Changes in the stability of the various aggregates upon variation of the surfactant structure will be largely discussed in terms of changes in the packing parameter *P*.



Experimental Section

Materials. The preparation and characterization of **1–22** have been described previously.[9] Surfactant **27** has been synthesized according to a general procedure.[11] The 1-methyl-4-(alkoxycarbonyl)pyridinium iodides **23–26** were prepared according to Hundscheid et al.[12] Isonicotinic acid and the corresponding alkyl iodides were used as received. 1-Iodotetradecane was synthesized in 85% yield[13] from the corresponding bromide by reflux with an excess of NaI in acetone for 24 h. *n*-Decyl- and *n*-dodecyl-4-pyridinecarboxylate were liquids at room temperature. These pyridine derivatives were purified by crystallization from acetone at low temperature. The surfactants **23–26** possess thermotropic liquid-crystalline properties and their complex melting behavior will be discussed separately.[14] Surfactant **26** has been described previously.[12]

1-Methyl-4-[(*n*-decyloxy)carbonyl]pyridinium Iodide (23). ^{1}H NMR: δ 0.81 (3 H, t), 1.21 (14 H, b), 1.73 (2 H, qi), 4.35 (2 H, t), 4.74 (3 H, s), 8.42 (2 H, d), 9.55 (2 H, d). ^{13}C NMR: δ 13.9 (q), 22.4 (t), 25.5 (t), 28.2 (t), 28.9 (t), 29.0 (t), 29.2 (t), 31.6 (t), 50.0 (q), 67.5 (t), 127.1 (d), 144.3 (s), 146.8 (d), 161.1 (s). Anal. Calcd for $C_{17}H_{28}NO_2I$: C, 50.38; H, 6.96; N, 3.46; I, 31.31. Found: C, 50.36; H, 7.06; N, 3.52; I, 31.39.

1-Methyl-4-[(*n*-dodecyloxy)carbonyl]pyridinium Iodide (24). ^{1}H NMR: δ 0.79 (3 H, t), 1.18 (18 H, b), 1.71 (2 H, qi), 4.33 (2 H, t), 4.72 (3 H, s), 8.41 (2 H, d), 9.52 (2 H, d). ^{13}C NMR: δ 13.9 (q), 22.4 (t), 25.6 (t), 28.2 (t), 28.9 (t), 29.1 (t), 29.2 (t), 29.4 (t), 31.6 (t), 50.1 (q), 67.5 (t), 127.1 (d), 144.3 (s), 146.8 (d), 161.1 (s). Anal. Calcd for $C_{19}H_{32}NO_2I$: C, 52.66; H, 7.44; N, 3.23; I, 29.28. Found: C, 52.48; H, 7.49; N, 3.27; I, 29.20.

1-Methyl-4-[(*n*-tetradecyloxy)carbonyl]pyridinium Iodide (25). ^{1}H NMR: δ 0.86 (3 H, t), 1.24 (22 H, b), 1.75 (2 H, qi), 4.41 (2 H, t), 4.80 (3 H, s), 8.47 (2 H, d), 9.53 (2 H, d). ^{13}C NMR: δ 13.9 (q), 22.4 (t), 25.5 (t), 28.1 (t), 28.9 (t), 29.1 (t), 29.2 (t), 29.4 (t), 31.6 (t), 50.0 (q), 67.5 (t), 127.0 (d), 144.3 (s), 146.8 (d), 161.1 (s). Anal. Calcd for $C_{21}H_{36}NO_2I$: C, 54.66; H, 7.86; N, 3.04; I, 27.50. Found: C, 54.65; H, 7.91; N, 2.95; I, 27.51.

^{1}H NMR Spectroscopy. Line widths at peak half-height ($\Delta\nu_{1/2}$) and peak splittings were calculated from ^{1}H NMR spectra of the aggregates in D_2O, using a Bruker WH-90-DS (90 MHz) or a Nicolet NT-200 (200 MHz) spectrometer operating in the FT mode.

Electron Microscopy. The samples were examined on a Philips EM 300 electron microscope operating at 80 kV. Carbon-coated Formvar grids, pretreated by glow discharge in air (sometimes 1-aminopentane), were used as matrices. Aliquots of vesicle solutions were stained with a 1% (w/v) solution of the required dye. For the freeze–fracture electron microscopic measurements the vesicle solutions were quickly frozen in liquid freon and freeze-fractured in a Balzer freeze etch unit according to the method described by Moore.[15]

(11) Sudhölter, E. J. R.; Engberts, J. B. F. N. *J. Phys. Chem.* **1979**, *83*, 1854.
(12) Hundscheid, F. J. A.; Engberts, J. B. F. N. *J. Org. Chem.* **1984**, *49*, 3088.
(13) Jones, L. W.; Powers, D. H. *J. Am. Chem. Soc.* **1924**, *46*, 2518.
(14) Nusselder, J. J. H.; Engberts, J. B. F. N.; van Doren, H. A. Submitted for publication.
(15) Moore, H. Z. *Zellforsch.* **1964**, *62*, 546.

Table I. Surfactant and Aggregate Properties of 1-Methyl-4-(C_{12}-alkyl)pyridinium Halides

surfactant	P^* [a]	aggregate morphology[b]	crc,[c] mmol kg^{-1}	crc/cmc[g]
1	0.36	SM	>657	>15
2	0.36	SM-RM	122	11
3	0.36	SM-RM	57	11
4	0.36	SM-RM	45	18
5	0.36	SM-RM	*d*	*d*
6	0.53	SM-RM	25	6
7	0.58	SM-RM	30	8
8	0.86	SM-V	18[e,h]	4
9	0.91	M-V	8.70[e,f,i]	
10	0.87	M-V	2.68[e,f,i]	
11	0.81	M-V	2.77[e,f,i]	
12	0.29	SM	>440	>106
21		SM-RM	ca. 600	ca. 121
22		SM-RM	25	7

[a] Apparent packing parameter, see text. [b] M = monomer, SM = spherical micelle, RM = rodlike micelle, V = vesicle. [c] In D_2O at 30 °C. [d] Krafft temperature in D_2O is higher than 30 °C. [e] cvc. [f] In H_2O at 25 °C. [g] The cmc's (in H_2O) were taken from ref 9. [h] Obtained from ^1H NMR. [i] Obtained from conductivity.

Vesicle Preparation. Vesicles were prepared by the ethanol injection method[16] or by the sonication method.[17] Thus, for the first method, the surfactant (5–10 mg) was dissolved in 100 μL of 96% ethanol. Small aliquots (80 μL) of this solution were injected into 2 mL of double-distilled water at 50 °C using a preheated microsyringe (60 °C). In the second method a suspension of bilayer fragments in aqueous solution was transformed into vesicles by sonication for 10–20 min at 50 °C under a stream of nitrogen by means of a pulsed high energy probe (Branson Sonifier Cell Disruptor B15).

Turbidity Experiments. The transmission (T, %) of solutions was monitored at 400 or 450 nm on a Perkin-Elmer λ5 UV–vis spectrophotometer.

Solubility Experiments. An aqueous suspension of surfactant was heated until the crystals in solution were dissolved. This solution was stirred for at least 24 h at 30 °C. After filtration, the concentration of the surfactant in the filtrate, the critical vesicle concentration (cvc), was determined by using Lambert–Beer's law (λ = 274 nm, ε = 3682).

Absorption Spectroscopy and Conductivity Experiments. Experimental details have been described previously.[9]

Results and Discussion

At a critical concentration in aqueous solution, surfactant monomers associate and various properties change in a characteristic manner. However, the morphology of the aggregate cannot be derived from these changes.[9] In this study, the morphology of the aggregate was monitored by a combination of ^1H NMR spectroscopy, turbidity experiments, and electron microscopy. The line widths at peak half-height ($\Delta\nu_{1/2}$) of all C–H resonances of surfactants organized in rodlike micelles or vesicles are broad[18] compared to those of spherical micelles. By monitoring $\Delta\nu_{1/2}$ as a function of the surfactant concentration, the critical rod concentration (crc) or the critical vesicle concentration (cvc) can be measured. Electron microscopy discriminates between rodlike micelles and vesicles. Furthermore, at the cvc surfactant monomers pack primarily into bilayer fragments that scatter light. These fragments can be transformed into vesicles by heating or sonication.[17] Alternatively, vesicles can be made directly by the ethanol injection technique.[16]

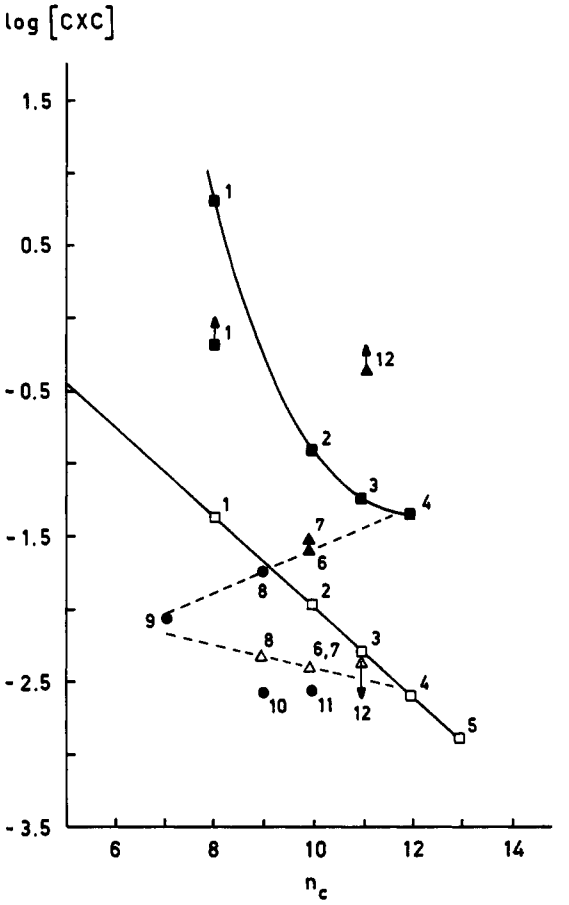


Figure 1. Plots of log [cxc] vs n_c (see text) for aggregates formed from 1–12 (30 °C). Unbranched surfactants: □, cmc; ■, crc. Branched surfactants: △, cmc; ▲, crc; ●, cvc.

1-Methyl-4-(or 2-)alkylpyridinium Halides. Table I lists the crc (and the crc/cmc ratio) of 2–7 and 21–22. The mean error is about 1 mmol kg^{-1}. The apparent packing parameters (P^*) of the relevant surfactant monomers are also presented in this table. The P^* values were calculated from CPK models assuming complete counterion binding and no headgroup hydration. This parameter will be proportional but *not* equal to the packing parameter defined by Israelachvili.[10]

It appears that the crc is strongly dependent on the number of carbon atoms in the main chain (n_c) in unbranched 1-methyl-4-alkylpyridinium iodide surfactants 1–5. The crc also depends on the degree of branching in 1-methyl-4-(C_{12}-alkyl)pyridinium iodide surfactants 4 and 6–7.

For the branched surfactant 8 a rather unique transition of spherical micelles into vesicles was observed at 18 mmol kg^{-1}. For 9–11 a turbid solution is formed at the cvc, which can be transformed into vesicles (diameters 107–120 nm, measured by electron microscopy). The cvc's of 8–11 are listed in Table I.

A decrease in n_c results in a dramatic increase in the crc (compare 1–4, Figure 1), although P^*, i.e., the shape of the surfactant does not change. This dependence of the crc on n_c is, however, generally found for ionic surfactants.[19] The growth of spherical micelles into rodlike micelles can be described in terms of the ladder model.[20] Missel et

(16) Kremer, J. M. H.; van de Esker, M. W. J.; Pathmamanoharan, C.; Wiersema, P. H. *Biochemistry* **1977**, *16*, 3932.
(17) Fendler, J. H. *Acc. Chem. Res.* **1980**, *13*, 7.
(18) (a) Nery, H.; Marshal, J. P.; Canet, D. *J. Colloid Interface Sci.* **1980**, *77*, 174. (b) Kalyanasundaram, K.; Grätzel, M.; Thomas, J. R. *J. Am. Chem. Soc.* **1975**, *97*, 3915.
(19) Missel, P. J.; Mazer, N. A.; Benedek, G. B.; Carey, M. C. *J. Phys. Chem.* **1983**, *87*, 1264.
(20) (a) Missel, P. J.; Mazer, N. A.; Benedek, G. B.; Young, C. Y.; Carey, M. C. *J. Phys. Chem.* **1980**, *84*, 1044. (b) Missel, P. J.; Mazer, N. A.; Carey, M. C.; Benedek, G. B. *J. Phys. Chem.* **1989**, *93*, 8354.

al.[19,20] have shown for spherical micelles formed from unbranched alkyl sulfates that the large variation in the tendency of these micelles to grow upon variation in the alkyl chain length is solely the result of the change in the aggregation number of the *spherical* micelle. For this series of alkyl sulfate surfactants the aggregation number of the spherical micelle is only dependent on the length of the alkyl chain.[19] The ladder model provides also a reasonable description for the growth of 1-methyl-4-alkylpyridinium iodide micelles.[21] Using this model, the crc's of **2–4**, and the aggregation numbers of the spherical micelles,[22] a crc for **1** of about 6.4 M can be estimated. Thus, the large differences in crc for **1–5** are due exclusively to differences in the aggregation number of the spherical micelles.

The unbranched surfactants **1–5** initially aggregate to form spherical micelles. This is in accord with the finding that P^* does not change with the alkyl chain length. Therefore, it must be concluded that the aggregate morphology does not depend on n_c, as predicted by Israelachvili.[10] Elongation of an unbranched alkyl chain only increases the *stability* of the aggregate (either a micelle or a vesicle).

There is a large change in the ratio crc/cmc upon variation of n_c. However, this ratio does not give a real indication for the propensity of growth. From this ratio one may conclude that the tendency for growth of **4** is less than that of **2** and **3** (Table I). From crc/cmc ratios presented in the literature,[23] one may conclude that the tendency for growth of spherical micelles composed of short-chain ionic surfactants is *higher* than that for micelles composed of long-chain surfactants. Both conclusions are certainly not valid.

Alkyl chain branching in the 1-methyl-4-(C_{12}-alkyl)-pyridinium iodide surfactants **4**, **6**, **7**, and **12** alters the propensity for growth dramatically. The tendency to grow, which according to the ladder model[20,21] is related to (crc/cmc), is clearly dependent on the position and the degree of branching. The P^* value, a measure for the shape of a surfactant monomer, and the tendency to grow show an approximate correlation. Branching near the headgroup (**12**) results in a change in the conformation of the alkyl chain near the headgroup[8] and increases the headgroup area. This is expressed in a decrease of P^* to 0.29. For the spherical micelles formed from **12**, there is no indication for a transition into rodlike micelles at surfactant concentrations as high as 0.44 M. Branching near the chain end (**6** and **7**) increases P^* (Table I) and makes the spherical micelles more prone to grow as compared to those of **4**. Alkyl chain branching shortens the alkyl chain length if the total number of carbon atoms in the alkyl chain is kept constant. When the number of carbons in the main chain of a surfactant (n_c) decreases, the aggregation number of the spherical micelle becomes lower.[22,24] However, the crc's of these types of branched surfactants decrease upon decreasing n_c (Figure 1), in contrast to unbranched surfactants. Most likely, the more conelike shape of the branched surfactants **6** and **7** results in higher P^* values and enhances the propensity to pack into a cylinder. These factors hide the effect of the decrease of the aggregation number.

Table II. crc or cvc of 1-Alkyl-4-*n*-dodecylpyridinium Iodide Surfactants

surfactant	1-alkyl chain	transition[a]	[cxc],[b] mmol kg^{-1}
4	Me	SM–RM	45
14	Et	SM–RM	38
15	*n*-Pr	SM–RM	28
16	*i*-Pr	SM–RM	30
17	*n*-Bu	SM–V	4–5[c]
18	*n*-Hex	M–V	0.78–0.85[c]
19	$(CH_2)_3OH$	SM–V	4.51[c]
20	$(CH_2)_2OCH_3$	SM–RM	39

[a] M = monomer, SM = spherical micelle, RM = rodlike micelle, V = vesicle. [b] cxc = crc in D_2O at 30 °C unless stated otherwise. [c] cvc in H_2O at 30 °C.

For the even more branched surfactants **8–11** a markedly different aggregation behavior is observed. Surfactants **9–11** aggregate into bilayers. The exact morphology of the aggregate of **8** at surfactant concentrations beyond 18 mmol kg^{-1} is not entirely clear. Negative-staining and freeze–fracture electron microscopy reveal large multilamellar and some small unilamellar vesicles. In any case, the aggregation behavior of **8–11** is completely different from that of **4**, **6**, **7**, and **12**. In fact, this was anticipated since the P^* values calculated for these surfactants are much higher. However, it seems clear that P^* values are not appropriate to describe the rather subtle differences in aggregation behavior of **8** compared to those of **9–11**.

From Figure 1 it emerges that there is a linear dependence of n_c on log [cxc] for **4** and **6–9** (correlation coefficient 0.986). The physical significance of this dependence is not clear at the moment.

The effect of the presence of a stiff acetylenic segment in the 4-alkyl group (**13**) has been discussed previously.[7] Changing the position of the alkyl chain from the 4- to the 2-position in the pyridinium ring (**4** vs **22**) decreases the crc. Exchange of the counterion from I^- (**4**) to Br^- (**21**) strongly inhibits micellar growth. The crc of **21** is ca. 13 times larger than that of **4**. The changes in the cmc are much less.[9] Furthermore, the sphere-to-rod transition of **21** is much less cooperative than that of **4**. The literature reveals a similar picture.[25] The use of smaller counterions increases the effective charge of the headgroup in the aggregate. This hampers micelle formation and decreases the value of P and, concomitantly, the tendency to grow. However, since the headgroups are closer together in rodlike micelles than in spherical micelles, the latter process is more strongly hampered, and therefore the crc is much more sensitive to changes in the counterion than is the cmc.

1-Alkyl-4-*n*-dodecylpyridinium Iodides. Variation of the 1-alkyl group in 1-alkyl-4-*n*-dodecylpyridinium iodide surfactants leads to remarkable differences in aggregation behavior. Spherical micelles grow into rodlike micelles for **4**, **14–16**, and **20** or into bilayer membranes for **17** and **19** (Table II). Monomers of **18** aggregate directly into bilayer membranes, which can be easily transformed into vesicles. The crc or cvc values of the various 1-alkyl-4-*n*-dodecylpyridinium iodides are listed in Table II.

For the surfactants **4** and **14–16** the crc decreases with increasing hydrophobicity of the alkyl chain and log crc is linearly dependent on the hydrophobicity of the 1-alkyl group expressed in the sum of Rekker's hydrophobic fragmental constants.[26] The 1-alkyl chain of **4** and **14–16**

(21) Nusselder, J. J. H.; Engberts, J. B. F. N. Submitted for publication.
(22) Binana-Limbele, W.; Zana, R.; Nusselder, J. J. H.; Engberts, J. B. F. N. To be published.
(23) (a) Porte, G.; Poggi, Y. *Phys. Rev. Lett.* **1978**, *41*, 1481. (b) Alauddin, M.; Rao, N. P.; Verrall, R. E. *J. Phys. Chem.* **1988**, *92*, 1301. (c) DeLisi, R.; Fiscaro, E.; Milioto, S.; Pelizzetti, E.; Savarino, P. *J. Solution Chem.* **1990**, *19*, 247.
(24) Caponetti, E.; Triolo, R.; Ho, P. C.; Johnson, J. S., Jr.; Magid, L. J.; Butler, P.; Payne, K. A. *J. Colloid Interface Sci.* **1987**, *116*, 200.
(25) Abe, A.; Imae, T.; Ikeda, S. *Colloid Polym. Sci.* **1987**, *265*, 637.
(26) Rekker, R. F. *The Hydrophobic Fragmental Constant*; Elsevier: Amsterdam, 1977; pp 350–355.

will not fold back into the core of the aggregate[4,9,27] and the packing parameter will remain constant or will slightly decrease.[4]

In contrast to the spherical micelles formed from 4 and 14–16, those of 17, in which the 1-alkyl group is an *n*-butyl group, are transformed into a lamellar phase when the surfactant concentration is increased above the cvc. Sonification provides vesicles (diameter 50–160 nm) as evidenced by negative staining electron microscopy. Since the packing parameter will increase significantly upon backfolding of an *n*-butyl chain, preferential bilayer formation is anticipated. Obviously the longer *n*-hexyl substituent in 18 also folds back since the monomers of 18 aggregate directly into a lamellar phase. No details are known yet about the exact chain packing in these vesicles. However, interdigitation of the alkyl chains to optimize the van der Waals interactions may well be assumed, similar to the chain packing in asymmetric phosphocholine bilayers[28] and in vesicles formed from highly asymmetric di-*n*-alkyl phosphates.[29]

Additional support for the importance of backfolding of the 1-alkyl chain in 1-alkyl-4-*n*-dodecylpyridinium iodide surfactants in promoting a transition into a lamellar phase can be derived from the aggregation behavior of 20. Spherical micelles of 20 grow into rodlike micelles and not into a lamellar phase although the length of the 1-alkyl group is similar to that in 17. Upon backfolding, the conformational energy of the 1-alkyl chain increases because of an increase in the number of gauche bonds. For hydrophobic 1-alkyl chains (17 and 18) this loss in energy will be compensated by the favorable free energy of transfer of (part of) the 1-alkyl chain from the Stern region into the core of the assembly. The 1-alkyl chain of 20 is more hydrophilic than that of 17, and therefore the driving force for backfolding will be much less or even absent. Thus the alkyl chain of 20 remains fully exposed to water, in contrast to that of 17. Transformation into a lamellar phase is now impossible and rodlike micelles are observed at higher surfactant concentrations.

Surfactant 19 also contains a hydrophilic 1-alkyl group. Unexpectedly, the spherical micelles of 19 transform into large, leaflet-like crystals above 4.5 mmol kg^{-1}. These can be transformed into vesicles as evidenced by negative-staining electron microscopy. At pH = 3, however, no vesicle formation is observed. Presumably, the packing of 19 into a bilayer is caused by *partial* deprotonation of the hydroxy groups. The headgroup area of the formed zwitterionic surfactant will then be smaller, the packing parameter larger, and packing into a bilayer will be favored.

1-Methyl-4-(*n*-alkoxycarbonyl)pyridinium Iodides. From the work of Hundscheid et al.,[12] it appears that the aggregation of 26 is interesting and, in fact, surprising. It was found that 26 aggregates into bilayer membranes as evidenced by negative-staining and freeze–fracture electron microscopy.[12] It is uncommon that a surfactant monomer with a single, unbranched, hydrocarbon chain associates into a bilayer (vide infra). Therefore, it was worthwhile to examine the aggregation of 23–25 and compare them to that of 26, in order to gain a better understanding of the peculiar aggregation behavior of 26. Interestingly, 23–24 aggregate directly into vesicles above the cvc. In aqueous suspensions of 25 and 26 crystals are present at 30 °C, which can be transformed into vesicles either by heating or by sonication. The presence of vesicles was revealed in all cases by negative-staining (uranyl acetate) electron microscopy. An aqueous suspension of 1-methyl-4-*n*-heptadecylpyridinium iodide (27) also contains crystals at 30 °C. However, all attempts to transform these crystals into vesicles failed. The cvc's of 23–26 are listed in Table III.

Table III. cvc and Degree of Counterion Binding (β) for 23–26 in Water at 30 °C

surfactant	cvc, mmol kg^{-1}	β, %
23	6.28[a]	80
24	1.85[a]	85
25	0.43[b]	
26	0.11[b]	

[a] From conductivity experiments. [b] From solubility experiments.

The aggregation behavior of unbranched 1-methyl-4-(*n*-alkoxycarbonyl)pyridinium iodide surfactants 23–26 contrasts strongly with that of the structurally related 1-methyl-4-*n*-alkylpyridinium iodides. For the latter type of surfactants, spherical micelles are formed independent of the alkyl chain length n_c (n_c = 8–17). At higher surfactant concentrations, these spherical micelles grow into rodlike micelles. Below the Krafft temperature hydrated surfactant crystals are observed. In view of these results, the formation of vesicles from 23–26 was not expected. Again the aggregate morphology is independent of n_c (n_c = 10–16). These results support the notion that the packing parameter and, concomitantly, the aggregate morphology are independent of the alkyl chain length. But it is quite unique that a single-chain surfactant possessing an alkyl chain of only *ten* carbon atoms associates into vesicles.[30]

From the cvc of 23–26, a ΔG^{mc} of −3.20 kJ mol^{-1} can be calculated[9] in which ΔG^{mc} is the free energy of transfer of a CH_2 group in the main chain of the surfactant from water to the core of the aggregate. This ΔG^{mc} value coincides within experimental error with the ΔG^{mc} value of −3.19 kJ mol^{-1} calculated for spherical micelles formed from 1-methyl-4-alkylpyridinium iodide surfactants.[9] The micropolarity in the Stern region of vesicles of 24 (as deduced from the position of the charge-transfer absorption band of the pyridinium iodide) is methanol-like (Z(vesicle) = 84.7; Z(MeOH) = 83.6)[31] and somewhat higher than that of vesicles formed from various 1-methyl-4-(C_{12}-alkyl)-pyridinium iodides (Z(vesicle) = 80.5; Z(EtOH) = 79.6).[9]

From the results discussed above, it appears that 1-methyl-4-(alkoxycarbonyl)pyridinium iodides are very decently behaving surfactants. Both the ΔG^{mc} value and the micropolarity of the Stern region do not deviate significantly from those of structurally related surfactant systems. Nevertheless, 23–26 aggregate into bilayer membranes, in contrast to 1–5 and 27. This association into bilayers stems from either a higher packing parameter for 23–26, which results from a smaller headgroup area of the surfactant monomers in the aggregates, or from interdigitation of the alkyl chains according to Figure 2. It is speculated that the packing of the alkyl chains in this interdigitated bilayer is special, since the chain ends are in contact with the headgroups. The geometrical constraint to pack into this interdigitated bilayer is $l_c a_o \geq 2v$ and, therefore, bilayer can be formed if $P \leq {}^1/_2$. Unfortunately, neither the headgroup area nor the thickness of

(27) Zana, R. *J. Colloid Interface Sci.* **1980**, *78*, 330.
(28) Mattai, J.; Scripada, P. K.; Shipley, G. G. *Biochemistry* **1987**, *26*, 3287.
(29) Wagenaar, A.; Rupert, L. A. M.; Engberts, J. B. F. N.; Hoekstra, D. *J. Org. Chem.* **1989**, *54*, 2638.
(30) Compare: (a) Kunitake, T.; Okahata, Y.; Shimomura, M.; Yasunami, S.-I.; Takarabe, K. *J. Am. Chem. Soc.* **1981**, *103*, 5401. (b) Hargreaves, W. R.; Deamer, D. W. *Biochemistry* **1978**, *17*, 3759.
(31) Kosower, E. M. *J. Am. Chem. Soc.* **1958**, *80*, 3253.

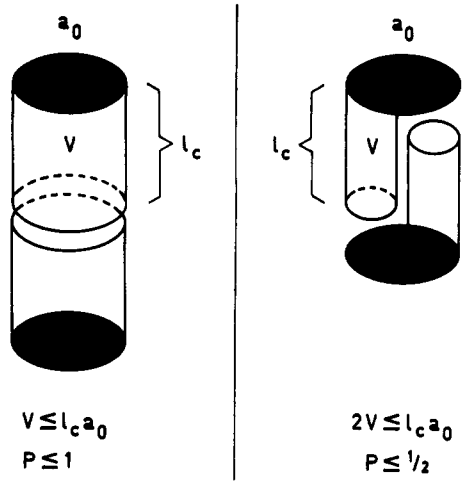


Figure 2. Relationship between the molecular dimensions of a surfactant monomer and the packing parameter (P) for packing in a normal bilayer (left) and in a special (see text) interdigitated bilayer (right).

the bilayer are known. However, we favor the second explanation, since the presence of the hydrophilic ester group will probably induce an increase of the headgroup area, facilitating interdigitation, rather than a decrease of the headgroup area.

Conclusions

The results described in this paper indicate that the morphology of a surfactant aggregate is mainly determined by the shape of the surfactant monomer. This dependence can be quantified by the packing parameter approach, as suggested by Israelachvili[10] for linear compounds. However, a novel combination of the approach of Israelachvili with the ladder model is necessary to understand the dependence of the aggregate type on the surfactant concentration. Thus, in summary: surfactants with $P \leq 1/3$ associate into spherical micelles that do not grow upon increasing surfactant concentration; surfactants with $1/3 < P \leq 1/2$ associate into spherical micelles that grow upon increasing surfactant concentration; and surfactants with $1/2 < P \leq 1$ aggregate into bilayers. The morphology of the aggregate does not depend on the alkyl chain length (n_c), although the thermodynamic stability of the aggregate is affected. The dependence of the crc on n_c solely originates from the dependence of the aggregation number of the spherical micelle on n_c.

The possibility for backfolding determines the morphology of the aggregate in cases where the headgroup substituent (1-alkyl chain) is varied and the 4-alkyl chain is kept constant (n-dodecyl). Preferential bilayer formation is found when backfolding occurs; otherwise spherical micelles are formed that grow into rodlike micelles at increasing surfactant concentrations.

Surfactants associate into bilayers instead of micelles when an ester group is inserted between the unbranched 4-alkyl chain and the pyridinium ring. Interdigitated packing of the alkyl chains, resulting in a change of the geometrical constraints for packing into a bilayer, is probably the origin for this remarkable aggregation behavior for an unbranched, single-chain surfactant.

Acknowledgment. The investigations were supported by the Netherlands Foundation for Chemical Research (SON) with financial aid from the Netherlands Foundation for Scientific Research (NWO). We thank Dr. M. Veenhuis and J. Zagers of the Biological Centre and J. F. L. van Bremen of the Biochemistry Department for the EM measurements.

Mechanisms of Macrocycle Genesis. The Condensation of Resorcinol with Aldehydes[1]

Frank Weinelt*,† and Hans-Jörg Schneider*,‡

Fachrichtung Organische Chemie der Universität des Saarlandes, D-6600 Saarbrücken 11, and Sektion Chemie der Karl-Marx-Universität, Leipzig, Germany

Received December 11, 1990

The title reactions proceed in high yields without high dilution techniques as long as substituents allow hydrogen bonds between the phenolic units and do not lead to steric hindrance. Isomerization rates for three epimeric cyclophanes, including a hitherto undiscovered one, are obtained by least-squares fit with integrated rate equations. The buildup sequences of oligomers, polymers, and macrocycles are analyzed by numerical stepwise integration with 50 rate constants, based on the fit of time–concentration curves of seven identified structures that were followed by proton NMR. Macrocyclization is favored by the following: (a) fast degradation of oligomers, (b) fast ring closure of tetramers, as well as (c) fast chain growth to these in comparison to ring opening. Homogeneous reaction conditions, here with methanol as solvent, are essential not only for the quantitative analyses, but also for the solubility of polymers in view of their degradation and for the observation of new stereoisomers. Molecular mechanics calculations with the CHARMm field and model considerations identify the factors responsible for the unique preference for cyclization over polymerization. Both hydrogen bonds between the phenolic units *and* 1.5 interactions between phenolic groups and the methyl substituent—stemming from the acetaldehyde—strongly favor folded conformers with small distances around d = 3.3–4.6 Å between the terminal reacting centers in comparison to stretched conformations with d = 12.2–18.3 Å.

The development of supramolecular chemistry and in particular its practical application depends to a considerable degree on the synthetic availability of macrocyclic host compounds in sufficient quantities. In spite of impressive recent advances,[2] the preparation of such macrocycles often requires application of high dilution prin-

† Karl-Marx-Universität (present address: Hoechst AG, D-W 8269 Burgkirchen 2, FRG).
‡ Universität der Saarlandes.

(1) Part 27 of the Saarbrücken series in Host-Guest chemistry. Part 26: Schneider, H.-J. et al. In *Frontiers in Supramolecular Chemistry and Photochemistry*; Schneider, H.-J., Dürr, H., Eds.; VCH: Weinheim, 1991.
(2) (a) Stoddart, J. F. In *Frontiers in Supramolecular Organic Chemistry and Photochemistry*; Schneider, H.-J.; Dürr, H., Eds.; Verlag Chemie: Weinheim, 1991.

0022-3263/91/1956-5527$02.50/0