gesting some degree of interaction of the radical with the metal). In contrast to these results, reduction of the iBC yields only a blue shift of the visible absorption band and an EPR spectrum diagnostic of Ni(I) with the electron added to the $d_{x^2-y^2}$ orbital: g = 2.064, 2.076, and 2.199 with average nitrogen hyperfine splittings of 11 G (four nitrogens).[13] These values are similar to those found for the Ni(I) complexes of F430 pentamethyl ester,[4] octaethyl iBC,[5] and tetraaza derivatives.[14]

The very negative reduction potentials of the compounds required that EXAFS measurements be carried out under strictly anaerobic conditions. This was accomplished with electrochemical cells[15] equipped with side arms for optical, EPR, and EXAFS measurements. The EXAFS arm is analogous to an optical cell but with aluminized Mylar windows epoxied to a glass frame. Such a cell readily held high vacuum, and optical, EPR, and EXAFS data could be acquired on the same sample.[13,16]

EXAFS data for the Ni(II) complexes and their reduction products are shown in Figure 1. Analysis[17] of the parent porphycene results yields Ni(II)–N distances of 1.89 (±0.02) Å, in good agreement with single-crystal X-ray data of 1.896 (±0.002) Å.[18] Reduction of the porphycene to its π anion radical leaves the geometry around the Ni virtually unchanged, as evidenced by the close similarity of the EXAFS spectra before and after reduction (Figure 1c,d). Not surprisingly, there is no evidence of coordination of the anion by the bulky Bu_4N^+ counterion. Similarly, the spectra of the chlorin and its anion radical do not differ, again indicating that the Ni environment remains unperturbed upon reduction (Figure 1a,b). Analysis of the parent chlorin spectrum yields average Ni–N distances of 1.95 (±0.02) Å. X-ray data for the compound are not available, but other Ni(II) chlorin structures have been reported:[19] Ni–N(pyrrole) distances range between 1.92 and 1.97 Å and Ni–N(pyrroline) bonds between 1.94 and 2.04 Å. The shorter distances are typically found in distorted chlorins.

Analysis[17] of the Ni(II) iBC EXAFS data yields average Ni–N distances of 1.93 (±0.02) Å. X-ray diffraction[6,20] data show the molecule to be severely distorted, with Ni–N distances of 1.920 (7), 1.902 (6), 1.925 (6), and 1.910 (7) Å, for an average distance of 1.915 Å. The EXAFS data for the Ni(II) iBC thus agree well with the crystallographic results. (No difference was found between the iBC in solution and amorphous samples.)

In contrast to the results obtained for the Ni(II) π radicals of the porphycene and the chlorin, the EXAFS spectra of the Ni(I) iBC differ significantly from those of the Ni(II) compound (Figure 1e,f). A satisfactory fit to the data[17] requires two sets of nitrogen distances of 1.85 (±0.05) and 2.00 (±0.03) Å. Hence, reduction to Ni(I) induces a distortion in the macrocycle core rather than a simple expansion.[21] X-ray results for another d^9 system, Cu(II) dioxo iBC,[22] show a similar bonding pattern: Cu–N distances = 2.035 (5), 2.053 (5), 2.006 (5), and 1.992 (5) Å.

Reduction of Ni(II) to Ni(I) thus requires that the macrocycle accommodate a change of ±0.1 Å in Ni–N bonds. Structural data certainly provide examples of such flexibility in hydroporphyrins.[19,23] Noteworthy, however, is our observation[6] that the hexahydro and octahydro derivatives in the homologous series[10] represented by the chlorin and iBC discussed above are *not* reduced to Ni(I), although the compounds are harder to reduce than the iBC. More extensive saturation may therefore render the macrocycles too rigid to accommodate the Ni(I) ion. This structural constraint may be less crucial in F430 itself. EXAFS studies[24] of the complex and its epimers yield Ni(II)–N distances ranging between 1.9 and 2.1 Å. Such macrocycle cores would thus readily accommodate the Ni(I)–N distances reported here.

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Supplementary Material Available: Details of the EXAFS experiments and fits and optical and EPR spectra of the Ni(II) chlorin anion radical and Ni(I) iBC anion (10 pages). Ordering information is given on any current masthead page.

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Bilayer-Forming Ion-Pair Amphiphiles from Single-Chain Surfactants[1]

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In this paper we show that amphiphilic ion pairs, derived from a series of trimethyl-*n*-alkylammonium bromides and saturated fatty acids, form vesicles upon sonic dispersal in water. We further show that the ability of such "ion-pair amphiphiles" (IPAs) to form a lamellar phase is critically dependent upon the absence of salts which can compete, effectively, for binding. Ion-pair amphiphiles of the type described herein are proposed as a novel class of vesicle-forming material for both theoretical investigations and practical device applications.[2]

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[1] Supported by Nagoya Municipal Industrial Research Institute (Grant 1989-01, H.F.) and by the National Science Foundation (Grant CHE-87-00833, S.L.R.).

[2] A recent report by Kaler et al. confirms our present findings that vesicles can be produced from mixtures of oppositely charged, single-chain surfactants: Kaler, E. W.; Murthy, A. K.; Rodriguez, B. E.; Zasadzinski, J. A. N. *Science* **1989**, *245*, 1371. Earlier work, with oppositely charged, single-chain surfactants, has also supported the existence of a lamellar phase: Jokela, P.; Jonsson, B.; Khan, A. *J. Phys. Chem.* **1987**, *91*, 3291.

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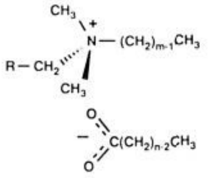
The geometry of a surfactant molecule is believed to play a critical role in defining its supramolecular properties. In simplest terms, conical-shaped surfactants maximize their intermolecular hydrophobic interactions by adopting micellar structures; i.e., they pack "most confortably" into spherical aggregates. In contrast, cylindrical-shaped surfactants prefer to assemble into bilayers. A classic example of the former is cetyltrimethylammonium bromide; zwitterionic phosphatidylcholines are biologically relevant examples of the latter.[3] Recently, it occurred to us that simple pairing of an amphiphilic single-chain cation with an amphiphilic single-chain anion might result in a novel vesicle-forming surfactant. Specifically, we reasoned that the effective interfacial headgroup area of each "partner" of an IPA should be substantially smaller than for each individual surfactant, due to electrostatic *attraction* between headgroups, and due to a reduction in hydration. The net effect would be an overall increase in the cylindrical character of each ion (Scheme I). In addition, we were intrigued with the close structural similarity between IPAs and the analogous phosphatidylcholines; i.e., both species are zwitterionic and both carry two long hydrocarbon chains. In principle, ionically paired single-chain surfactants could provide a means for "bridging the supramolecular gap" between single- and double-chain amphiphiles. Moreover, the ready availability and low cost of single-chain surfactants, as compared with double-chain analogues, provides an additional incentive for testing this hypothesis. Motivated by both theoretical and practical considerations, we have examined the feasibility of preparing vesicle structures from such surfactant pairs. This report describes our preliminary findings.

A series of IPAs **1a–d** were prepared by passage of the appropriate trimethyl-*n*-alkylammonium bromide through an ion-exchange resin (Bio-Rad, AG1-X8; hydroxide form), followed by (i) reaction with a stoichiometric quantity of the corresponding saturated fatty acid in methanol, (ii) evaporation of solvent under reduced pressure, and (iii) recrystallization from ethyl acetate. All IPAs reported herein were obtained as colorless crystals, having satisfactory elemental analyses. Examination by IR spectroscopy (KBr disk) confirmed the complete disappearance of the carboxylic acid moiety (1710 cm^{-1}) and the appearance of the ammonium carboxylate group (1560 cm^{-1}).



1a, m=n=14; R=H
b, m=n=16; R=H
c, m=n=18; R=H
d, m=n=18; R=CH_2CH_2OH

Sonication of **1a** and **1b** in pure water (3 mg/mL; cup horn; 70 °C, 10 min) afforded translucent dispersions that were stable for more than 48 h, as judged by their turbidity (450 nm). In contrast, **1c** yielded dispersions that precipitated within 1 h. An analogous IPA (**1d**), having a hydroxyethyl moiety incorporated in the headgroup, afforded translucent dispersions that were stable for more than 1 month. Passage of aqueous dispersions produced from **1a**, **1b**, and **1d** through a Sephadex G-50 column led to a ca. 80% recovery in the void volume (HPLC analysis). Examination of each sample by dynamic light scattering (Nicomp 270 instrument) and by transmission electron microscopy (JEOL JEM-2000 FX instrument; 2% uranyl acetate) showed the presence of particles ranging in diameter between 200 and 800 Å; discrete membrane walls, however, were not readily apparent from the latter. A dispersion of **1b**, which was prepared by ethanol injection into water and examined as a frozen-hydrated sample, also showed spherical particles ranging between 300 and 1000 Å diameter (Figure 1).

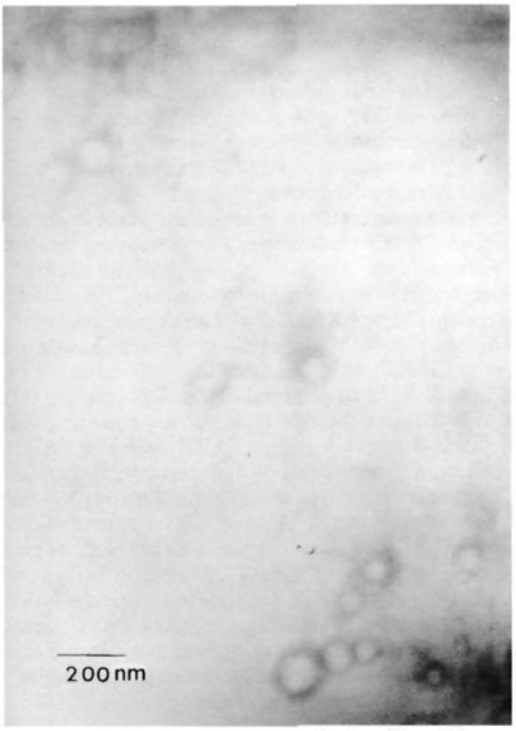


Figure 1. Transmission electron micrograph of vesicles of **1b**, prepared via ethanol injection and examined as a frozen-hydrated sample (−176 °C; Philips 400 TEM instrument).

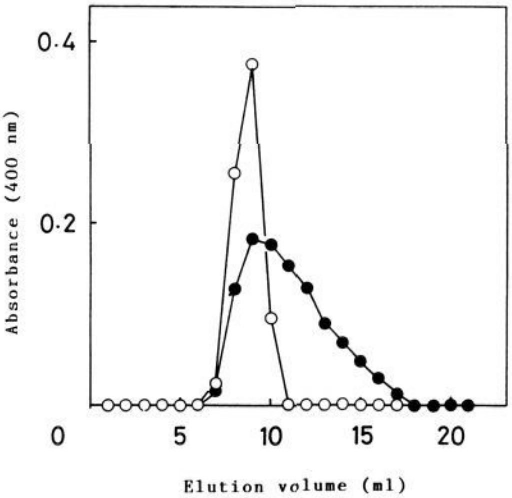


Figure 2. Gel filtration profile of **1b** (○) and a 1:1 molar mixture of cetyltrimethylammonium bromide plus sodium palmitate, (●) using a Sephadex G-50 column.

In an effort to confirm the presence of a lamellar phase, dispersions of **1a**, **1b**, and **1d** were investigated by differential scanning calorimetry (Seiko SSC/580 instrument). Well-defined phase transitions were readily observed for each dispersion, with apparent gel to liquid-crystalline phase-transition temperatures (T_c) of 20.5, 41.2, and 52 °C, respectively. It is noteworthy that these values parallel quite closely the T_c values that have been observed for those zwitterionic phosphatidylcholines having the exact same fatty acid chain length: dimyristoyl-*sn*-glycero-3-phosphocholine (23.9 °C), dipalmitoyl-*sn*-glycero-3-phosphocholine (41.4 °C), and distearoyl-*sn*-glycero-3-phosphocholine (54.9 °C).[4] Sonic dispersal of **1b** in water containing riboflavin, followed by removal of the nonentrapped marker, via gel filtration, and simultaneous mea-

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[3] Reviews: Evans, D. F. *Langmuir* **1988**, *4*, 3. Israelachvili, J. N.; Jarcelja, S.; Horn, R. G. *Q. Rev. Biophys.* **1980**, *13*, 121.

[4] Mabrey-Gaud, S. In *Liposomes: From Physical Structure to Therapeutic Applications*; Knight, C. G., Ed.; Elsevier/North Holland Biomedical Press: Cambridge, 1981; p 114.

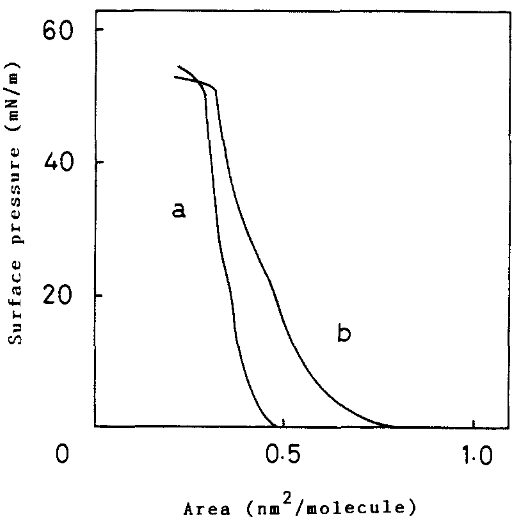
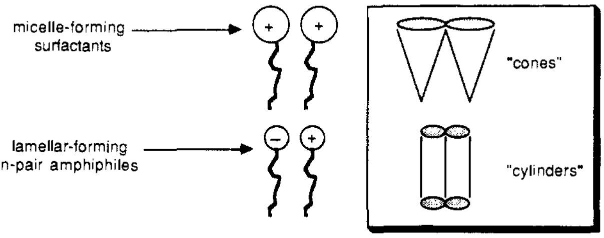


Figure 3. Surface pressure–area isotherms for (a) **1b** and (b) an equal molar mixture of cetyltrimethylammonium bromide plus palmitic acid (spread as one solution) at 20 °C. Monolayers were spread from benzene/ethanol (9:1, v/v) on a pure water subphase. Limiting areas, estimated by extrapolation to zero surface pressure, are 36 and 50 Å² for a and b, respectively.

Scheme I



surement of turbidity and fluorescence intensity, demonstrated that these microspheres contained an internal aqueous compartment. From such experiments, the captured volume was estimated to be 1.6 L/mol.[5]

Attempted vesicle formation by direct mixing of an equal molar mixture of cetyltrimethylammonium bromide and sodium palmitate in pure water (3 mg/mL) afforded a translucent dispersion that exhibited an apparent T_c of 41.0 °C. In sharp contrast to **1b**, however, its gel filtration profile was very broad, affording a 51% recovery in the void volume (fractions 7–11) and a 31% recovery in fractions 12–20 (Figure 2). These results infer the presence of both a vesicular and a micellar phase and also highlight the influence that salts and ion-exchange equilibria can exert on such systems. Comparison of the surface pressure–area isotherms measured for **1b** and for an equal molar mixture of cetyltrimethylammonium bromide plus palmitic acid also illustrates incomplete IPA formation at the air–water interface (Figure 3). The lower compressibility and smaller limiting area of **1b** are a likely consequence of tight ion pairing.

Ion-pair amphiphiles represent a new and unique class of vesicle-forming surfactants that warrant a detailed examination from both a theoretical and practical standpoint. Unlike conventional double-chain surfactants, however, special attention will have to be paid to the nature and concentration of all ionic species present in solution and to the appropriate ion-exchange equilibria. Studies that are now in progress are aimed at defining the full scope of IPAs and at the preparation of polymerizable analogues.

Acknowledgment. We are grateful to Michael Markowitz and Olga Shaffer (Lehigh) for valuable technical assistance.

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[5] The entrapment value given in the text has been corrected for an apparent adsorption of ca. 0.4 L/mol.

Replacing Apical-Substituent Methyl Groups by Trifluoromethyl Groups in 10-S-5 Hypervalent Sulfur Species Provides Less Acidic C–H Bonds on Equatorial Methyls[1,2]

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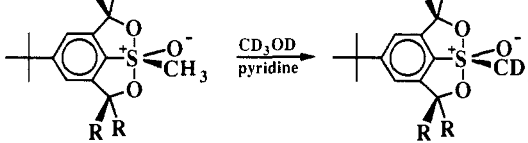
The substitution of a trifluoromethyl group for a methyl group has been found to increase the acidity of a labile proton of many acidic compounds.[3] The replacement of five methyl groups of pentamethylcyclopentadiene by trifluoromethyl groups was found by Laganis and Lemal[3c] to strongly stabilize the cyclopentadienyl anion, making the C–H proton of the cyclopentadiene more acidic than nitric acid. We find, however, that protons of the equatorial *S*-methyl group of a 10-S-5[2] sulfurane oxide are much reduced in acidity when the four methyl groups (R) adjacent to the apical oxygens (**1**) are replaced by trifluoromethyl groups (**2**).[4]



1 ($R = CH_3$)
2 ($R = CF_3$)
3 ($R = CH_3$)
4 ($R = CF_3$)

It was found earlier[6] that the equatorial methyl group of **1** was rapidly deuterated in CD_3OD at 25 °C. A solution of **1** and **2** in CD_3OD/pyridine at 25 °C showed within a few seconds, by NMR spectroscopy, complete deuteration of the equatorial methyl group of **1**, but no observable exchange for the fluorinated analogue **2** at that time. A much slower reaction (12 days at 25 °C) provided substantial deuteration of **2**. Deuterium exchange rates[7] are faster for **1** than for CF_3-substituted **2** by a factor of ca. 86 000 at 25 °C.

Deuteration of either **1** or **2** was catalyzed by an appropriate base, increasing the rate linearly relative to the base concentration. Easily measurable catalysis for **2** required a strong base such as sodium methoxide-d_3 ($pK_\alpha = 15.5$)[3a] in a solvent made of equal volumes of tetrahydrofuran-d_8 (THF-d_8) and CD_3OD. For sulfurane oxide **1**, in an equal volume mixture of CD_2Cl_2 and CD_3OD, the much weaker base with $pK_\alpha = 10.7$, potassium hexafluoro-2-phenyl-2-propoxide[8,9] [$KOC(CF_3)_2Ph$], provided

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[1] Rongione, J. C.; Martin, J. C. Presented in part at the 194th National Meeting of the American Chemical Society, New Orleans, LA, Sept 1987; paper ORGN 270.

[2] An *N*–X–*L* system formally involves *N* electrons in bonding *L* ligands to atom X. Perkins, C. W.; Martin, J. C.; Arduengo, A. J., III; Lau, W.; Alegria, A.; Kochi, J. K. *J. Am. Chem. Soc.* **1980**, *102*, 7753.

[3] (a) Serjeant, E. P.; Dempsey, B. *Ionization Constants of Organic Acids in Aqueous Solutions*; Pergamon Press: Oxford, 1979; Vol. 19, pp 23, 78, 10. (b) Kortum, G.; Vogel, W.; Andrusson, K. *Dissociation Constants of Organic Acids in Aqueous Solutions*; Butterworth: London, 1961; p 297. (c) Laganis, E. D.; Lemal, D. M. *J. Am. Chem. Soc.* **1980**, *102*, 6633.

[4] 2,6-Bis(1-hydroxy-1-(trifluoromethyl)-2,2,2-trifluoroethyl)-4-*tert*-butylbenzenethiol was methylated at sulfur with dimethyl sulfate and aqueous KOH.[5] Oxidation by *tert*-butyl hypochlorite provided 10-S-4 methylsulfurane in quantitative yield. Further oxidation to **2** (98%) used $RuO_2/NaIO_4$ in 1:1 *v*/*v* CCl_4/H_2O for 12 h at 25 °C. Although $KMnO_4$ is the oxidant used to form **1**, it does not oxidize the sulfurane precursor of the more electron deficient **2**.

[5] Perkins, C. W.; Wilson, S. R.; Martin, J. C. *J. Am. Chem. Soc.* **1985**, *107*, 3209.

[6] Lau, P. H.; Martin, J. C. *J. Am. Chem. Soc.* **1977**, *99*, 5490.

[7] Rates were determined in a 1:9 *v*/*v* CD_2Cl_2/CD_3OD solvent without added base. For **1**, rates were measured at −65 °C ($2.17 \times 10^{-4}\ s^{-1}$), −55 °C ($6.73 \times 10^{-4}\ s^{-1}$), and −39 °C ($2.43 \times 10^{-3}\ s^{-1}$) ($\Delta H^* = 8.36$ kcal/mol; $\Delta S^* = 34.2$ eu). The rate at 25 °C was then calculated to be $0.151\ s^{-1}$ for **1**. The rate of deuterium exchange for **2** ($1.75 \times 10^{-6}\ s^{-1}$) was measured in the same solvent at 25 °C.

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