Original disymmetric bolaforms bearing at least one sulfobetaine head; synthesis and surface properties

Souad Souirti and Michel Baboulène

Abstract: We describe a simple and efficient method for the synthesis of disymmetric bolaforms bearing at least one sulfobetaine head. In this process, we could introduce successively on α,ω-bis(dialkylamino) alkane a sulfobetaine head and a cationic, a sulfobetaine, or a carboxybetaine head, in excellent yield. This is the first synthesis of disymmetric sulfobetaine bolaforms. The method is easily generalized to various types of head functional groups. The wide range of bolaforms produced by this method has been exploited to study their surface properties and to determine the respective roles of the polar heads and the lengths of the spacers (*n*) on self-aggregation in aqueous media. A critical micellar concentration (cmc) was observed with the compounds with a spacer of 12 carbon atoms (*n* = 12). Micellization appeared to be consistent with a "wicket-like" conformation, which did not appear to form with the *n* = 8 compounds.

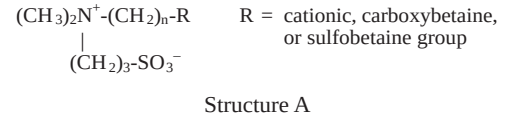
Key words: disymmetric bolaform, sulfobetaine, carboxybetaine, cationic amphiphile, synthesis, surface properties.

Résumé : Nous décrivons une simple et efficace méthode d'accés à des dissymmétriques bolaformes ayant au moins une tête sulfobétaine. Dans ce procédé nous pouvons introduire successivement sur les azotes d'un α,ω-bis(dialkylamino) alkane une tête sulfobétaine et une tête cationique ou sulfobétaine ou carboxybétaine avec d'excellents rendements. C'est la première synthèse de sulfobétaines bolaformes dissymétriques. La méthode décrite est facilement généralisable à diverses têtes polaires. La diversité des bolaformes ainsi obtenus permet d'aborder, à partir d'une étude tensiométrique, leurs propriétés de surface et de discuter du rôle des têtes polaires et de la distance entre les deux têtes (*n*) dans le mode d'aggrégation de ces composés en milieu aqueux. Les composés avec *n* = 12 se prêtent à la détermination d'une concentration micellaire critique (cmc). Leur micellisation semble en accord avec une conformation " en boucle" qui ne se retrouve pas pour les composés avec *n* = 8.

Mots clés : bolaforme disymmétrique, sulfobétaine, carboxybétaine, amphiphile cationique, synthèse, paramètres de surface.

Introduction

There have been a large number of descriptions of the synthesis of amphiphilic molecules, which self-aggregate into vesicles, as these compounds have a variety of application in chemistry and biochemistry (1, 2). Among the numerous families of surfactants, a novel architecture represented by the bolaform structure has been developed (3). Bolaforms are molecules bearing two polar heads separated by a hydrophobic chain of variable length. This structure lends itself to a modular synthesis of derivatives with different chains and polar heads. However, despite numerous reports on bolaforms, to our knowledge there are no descriptions of bolaforms with betaine heads. We have currently been investigating bolaforms derived from betaine (4). The encouraging preliminary results prompted us to examine derivatives with a sulfobetaine head. These compounds find applications as detergents and in cosmetics (5). Recently, Spencer et al. (6) have reported the inhibitory action of *N,N′*-bis[dimethylammonium-1-(4-butylsulfonyl)]dodecane, a sulfobetaine surfactant, on squalene synthetase. Nevertheless, the amphiphilic character of this compound was not conjured up, and we also know the importance of organized molecular systems into biological applications. Consequently, the bolaform structure open new perspectives for the surfactant chemistry. For this purpose, knowledge of the surface properties and comprehension of the process of vesicle formation will also require a number of derivatives for studying the self-aggregation behaviour. The interest of different polar heads at the ends of the hydrophobic chain is an added interest for such investigations.



Structure A

We present here a simple and general method for preparation of original disymmetric bolaforms bearing a sulfobetaine head with the other head being either cationic

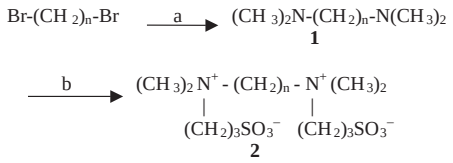
Received November 13, 2000. Published on the NRC Research Press Web site at http://canjchem.nrc.ca on August 3, 2001.

S. Souirti and M. Baboulène.[1] Laboratoire des Interactions Moléculaires et Réactivités Chimiques et Photochimiques, UMR (CNRS 5623) Université Paul Sabatier 118 route de Narbonne, 31062 Toulouse cédex 06 France.

[1]Corresponding author (telephone: 33 61 55 62 72; fax: 33 61 25 17 33; e-mail: mbab@ramses.ups-tlse.fr).

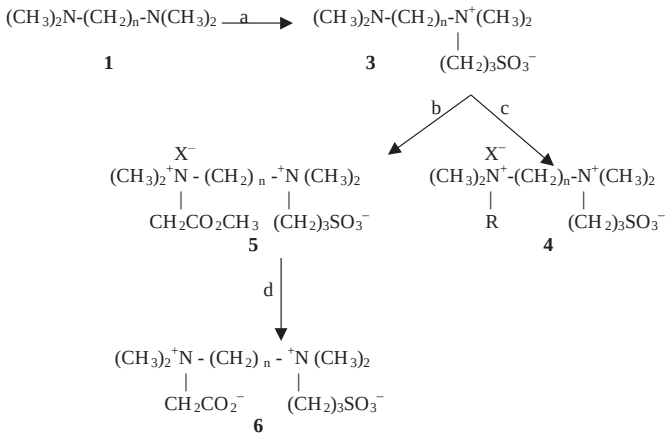
 DOI: 10.1139/cjc-79-7-1153

Scheme 1.



a: $HN(CH_3)_2$, ethanol/water, reflux;
b: 1,3-propane sultone, acetonitrile, reflux

Scheme 2.



a: 1,3-propane sultone, acetone, 15–20°C;
b: $BrCH_2CO_2C_2H_5$, methanol, reflux; *c*: RX, methanol, reflux, *d*: resin Amberlist™ OH^-, methanol, 20°C, 3 h.

or a betaine (structure A). The surface properties of the compounds prepared was then examined.

Synthesis

The sulfobetaine structure is readily produced by condensation of an amine with an alkylsultone (7). We employed this method using α,ω-bis(dialkylamino) alkane **1** according to Scheme 1.

This condensation reaction is quantitative. The sulfobetaines **2** are readily recovered with a high degree of purity by filtration because of the absence of by-products and the crystalline nature of the product. However, if the reaction mixture is heated, the reaction does not stop at the monocondensation product, but we did succeed in obtaining a quantitative yield of the monocondensed product **3** by using a large excess of sultone at a temperature of 15–20°C (Scheme 2). We have envisaged to take advantage of this particular reactivity. The compounds **3**, which are readily isolated in a pure state, can be utilized as intermediates in the synthesis of the disymmetric bolaforms (Scheme 2). The insertion of the second polar head is simple and easily generalized to various types of head.

Table 1 lists typical results that illustrate the possibilities of these novel synthons. This process should not be difficult to carry out on an industrial scale.

The bolaforms prepared were characterized from their IR and NMR spectra. It should be noted that the deshielding

Table 1. Yield and melting points of bolaforms prepared.

	n	R	X	Yield (%)	mp (°C)
2a	8	—	—	95	210
2b	12	—	—	96	218
3a	8	—	—	98	199
3b	12	—	—	98	230
4a	8	CH_3	I	95	225
4b	12	CH_3	I	95	222
4c	8	$C_{12}H_{25}$	Br	87	120
4d	12	$C_{12}H_{25}$	Br	87	105
4e	8	C_2H_5	Br	82	115
4f	12	C_2H_5	Br	80	125
5a	8	—	—	88	188–190
5b	12	—	—	83	170
6a	8	—	—	78	230
6b	12	—	—	75	260

Note: Calculated from Gibbs' equation (8).

observed on the chemical shifts of the $N\text{-}CH_3$ and $N\text{-}CH_2$ groups are consistent with quaternization of the nitrogen atom. Furthermore, the disymmetry of the polar heads was indicated by the differentiation of the ^{13}C NMR peaks of the $N\text{-}CH_3$ groups, which was further support for the proposed structures.

Surface properties

The surfactant properties of these novel bolaforms were studied by measuring interfacial tension (γ) in water, and calculated using the Gibbs' equation (8). The data are illustrated in Figs. 1 and 2 and listed in Table 2.

All compounds tested led to a marked reduction in interfacial tension at the air–water interface (30–35 mN m^{-1}). However, this action was found to depend on the concentration of the particular compound as a function of polar head and length of spacer. The compounds with $n = 12$ exhibited a break in the interfacial tension vs. concentration plots. This property of micellization occurred at relatively low values of critical micelle concentration (cmc), which shows promise for industrial applications.

We noted that the cmc value was strongly dependent on the nature of the polar head. The carboxy-sulfobetaine bolaform **6b** (cmc = 5.5 mM) was a better surfactant than the symmetrical sulfobetaine **2b** (cmc = 8.2 mM) or the carboxybetaine analogs (cmc = 6.7–8 mM (4)). On the other hand, the passage of carboxy-sulfobetaine **6b** to ammonium-sulfobetaine **5b** led to an increase in cmc (cmc = 18 mM). This can be accounted for by the stronger repulsion of the polar heads enhanced by steric interactions. Our findings are in line with those described for cationic bolaforms (12–18 mM (9)). Furthermore, these results were in accordance with those of the general literature; a spacer with $n = 8$ does not permit micellization. By contrast, we noted that introduction of a long alkyl chain onto the nitrogen atom led to a decrease in the cmc value. This was attributed to an increased hydrophobicity. For example, compound **4c** micellized at low concentration (cmc = 5 mM) despite the short spacer ($n = 8$), which is not generally compatible with micellization (9). The surfactants **4c** and **4d**, thus, represent

Fig. 1. Plots of interfacial tension (obtained by tensiometry) vs. log [bolaform] at 25°C in water.

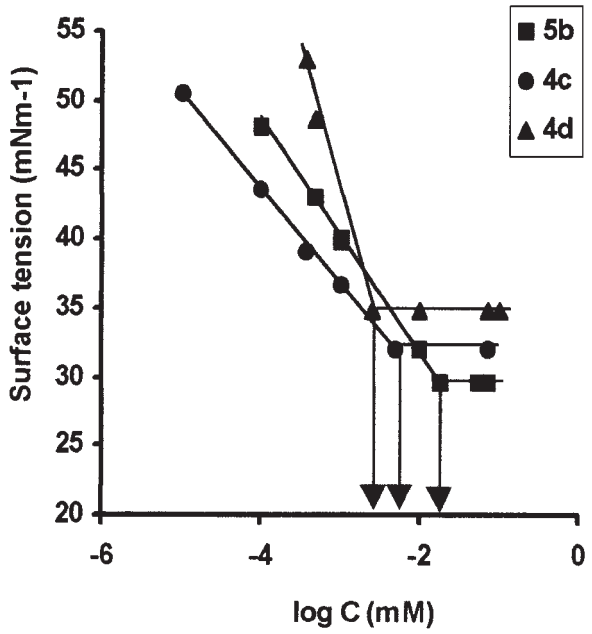
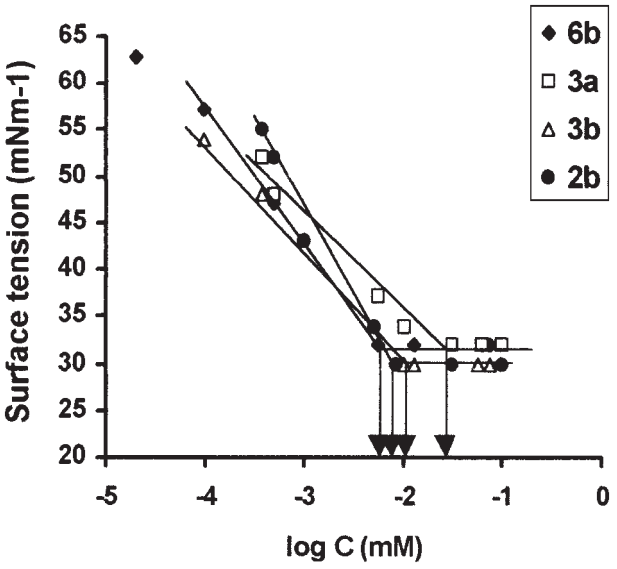


Fig. 2. Plots of interfacial tension (obtained by tensiometry) vs. log [bolaform] at 25°C in water.



a new family of surfactants as a hybrid between bolaforms and gemini surfactants (10). The synthesis proposed here is in keeping with the general pattern of the current research on the access to new potential surfactants. It was noteworthy that the presence of an iodine atom on the cationic head of the bolaforms **4a** and **4b** prevented micellization (at the concentrations studied = 10^{-1} M) even with a -$(CH_2)_{12}$- spacer (comparison **4b** and **4f**).

A number of comments can be made on the surface areas as calculated from the Gibbs' equation (8). The betaine bolaforms **6b** and **2b** occupy a space at the interface that is the arithmetic sum of the surface areas of the two polar heads (11, 12). These results are consistent with the length and flexibility of the spacer, which indicates that these surfactants adopt a " wicket-like" conformation at the air–water interface. By contrast, the calculated surface areas of the head of the disymmetric bolaforms **4d** (A = 188 Å^2) and **4f** (A = 167 Å^2) is slightly superior as the arithmetic sum of the calculated surface areas of the two polar heads (A ~ 130 Å^2) suggests the "wicked-like" conformation undergoes a flattening at the air–water interface. The presence of the methyl acetate group in compound **5b** (A = 252 Å^2) led significantly to flattening out of the molecule at the interface. A same arrangement was proposed for the bolaforms with a spacer n = 8 (see **4c**, A = 275 Å^2). This influence of the length of the hydrophobic chain was also demonstrated by comparison of the molecular areas of compounds **3a** with **3b**. This linear arrangement would be consistent with a more extended occupation of the interface. This type of molecular organization has been described for non-ionic (13) and cationic bolaforms.[2] On the other hand, it can envisage that these structures lead to a vesicular self-association. Further interpretations will have to await the results of light scattering and electron microscopic studies (in progress).

Table 2. Surface parameters of compounds in water at 25°C.

	γ (mN m^{-1})[a]	cmc (mM)	Γ (mol m^{-2})[a]	A (Å^2)[a]
2a	30[c]	—	—	—
2b	30	8.2	1.81×10^{-6}	91.56
3a	32	30	1.32×10^{-6}	125
3b	30	10	2.16×10^{-6}	77.6
4a	30.8[b]	—	—	—
4b	29.8[b]	—	—	—
4c	32	5	6.02×10^{-7}	275
4d	34.8	2.4	8.83×10^{-7}	188
4e	32[b]	—	—	—
4f	33	70	10×10^{-7}	167
5a	34[b]	—	—	—
5b	29.5	18	6.5×10^{-7}	252
6a	30[b]	—	—	—
6b	32	5.5	1.8×10^{-6}	92.26

[a] γ = interfacial tension by the stirrup detachment method.; Γ = superficial excess; A = area of the polar head.
[b] Obtained at [C] = 1×10^{-1} M.

Conclusion

We describe here a convenient route to disymmetric bolaforms bearing at least one sulfobetaine head, which could be scaled up for industrial applications. The method lends itself to a modular synthesis enabling preparation of a variety of derivatives with different polar heads and different spacers. To our knowledge, this is a first synthesis of sulfobetaine disymmetric bolaforms.

Our preliminary results on the surface properties of these bolaforms are encouraging, as they all led to a marked reduction in interfacial tension at the air–water interface at low concentrations. This surfactant action suggests that, by comparison with the well-known activity of other betaine surfactants, these bolaforms have potential applications as

[2] I. Rico-Lattes personal communication.

corrosion inhibitors. The role of the disymmetric head structure and the length of the spacers were demonstrated in micellar self-aggregation behaviour. Self-organization into vesicles is currently under investigation. Comprehension of their physicochemical properties will be facilitated by this convenient route to a wide range of derivatives of original disymmetric bolaform structure.

Experimental

General

Reagents were of commercial quality and were used without purification. IR spectra (ν, cm^{-1}) were recorded on a PerkinElmer 683 spectrophotometer. ^1H and ^{13}C NMR spectra (δ, ppm) were obtained on Bruker AC 80 or Bruker AC 200 instruments. Surface active properties were calculated using Gibbs' equation with the data obtained from measurements carried out Prolabo No. 3 tensima.

Typical procedure for the synthesis of compounds 1

A solution of dimethylamine (33% of ethanol) (3×10^{-2} mol) and dibromoalkane (1×10^{-2} mol) were added to a solution of sodium carbonate (2×10^{-2} mol) in ethanol (60 mL) and water (15 mL). The reaction mixture was heated at reflux and stirred for 24 h. Then the resulting compound was isolated by evaporating of the solvent under reduced pressure. The crude product washed with water (1×10 mL) was extracted with EtO_2.The organic phase was dried on anhyd Na_2SO_4 and evaporated in vacuo. The crude oil was purified by distillation.

*1,8-bis(*N,N- *dimethylamino)octane (**1a**)*

Yield: 98%. Colourless oil, bp 60°C, 0.06 mm Hg. ^1H NMR (200 MHz, $CDCl_3$) δ 1.1 (m, 12H, $(CH_2)_6$), 2.3 (t, 4H, NCH_2), 1.9 (s, 12H, NCH_3). ^{13}C NMR (200 MHz, $CDCl_3$) δ 27.2–28.3 ($(CH_2)_6$), 45.2 (NCH_3), 59.7 (NCH_2). Anal calcd. for $C_{12}H_{28}N_2$ (200.37): C 71.86, H 13.97, N 13.97; found: C 71.66, H 14.15, N 14.13.

*1,12-bis(*N,N-*dimethylamino)dodecane (**1b**)*

Yield: 98%. Colourless oil, bp 80–82°C, 0.05 mm Hg. ^1H NMR (200 MHz, $CDCl_3$) δ 1.1 (m, 20H, $(CH_2)_{10}$), 2.1 (t, 4H, NCH_2), 1.9 (s, 12H, NCH_3). ^{13}C NMR (200 MHz, $CDCl_3$) δ 27.4–28.5 ($(CH_2)_{10}$), 45.4 (NCH_3), 59.9 (NCH_2). Anal calcd. for $C_{16}H_{36}N_2$ (256.47): C 74.86, H 14.03, N 10.92; found: C 74.73, H 13.90, N 11.62.

Typical procedure for the synthesis of compounds 2

Compounds **2** were prepared by the addition of diamine **1** (1×10^{-2} mol) to 1,3-propane sultone (2.2×10^{-2} mol) in anhyd acetonitrile (100 mL). The solution was stirred at reflux for 4 h, then cooled and filtered. After crystallization from methanol–acetone (1:9), pure compounds **2** were obtained as solid, which decomposed during melting point determination.

*1,8-bis(*N,N- *dimethylammonio*-N-*propyl-1-sulfonate)octane (**2a**)*

Yield: 95%. White powder, mp 210°C. IR (KBr) (cm^{-1}): 1480 (C-N^+), 1040 (S=O). ^1H NMR (200 MHz, D_2O) δ 1.2 (m, 12H, $(CH_2)_6$), 1.9 (qt, 4H, CH_2-C-SO_3), 2.9 (t, 4H, CH_2SO_3), 3.0 (s, 12H, NCH_3), 3.2 (t, 4H, CH_2N), 3.4 (t, 4H, CH_2N). ^{13}C NMR (200 MHz, D_2O) δ 20.7–31.1 ($(CH_2)_6$), 49.8 (CH_2-C-SO_3), 53.1 (NCH_3), 64.4 (NCH_2), 66.7 (CH_2SO_3). Anal calcd. for $C_{18}H_{40}N_2O_6S_2$ (444.64): C 48.62, H 9.07, N 6.30, S 14.42; found: C 48.96, H 9.30, N 5.94, S 13.97.

*1,12-bis(*N,N- *dimethylammonio*-N-*propyl-1-sulfonate)dodecane (**2b**)*

Yield: 95%. White powder, mp 215°C. IR (KBr) (cm^{-1}): 1480 (C-N^+), 1040 (S=O). ^1H NMR (200 MHz, D_2O) δ 1.2 (m, 20H, $(CH_2)_{10}$), 2.2 (qt, 4H, CH_2-C-SO_3), 2.6 (t, 4H, CH_2SO_3), 3.0 (s, 12H, NCH_3), 3.2 (t, 4H, CH_2N), 3.3 (t, 4H, CH_2N). ^{13}C NMR (200 MHz, D_2O) δ 20.7–31.1 ($(CH_2)_{10}$), 49.8 (CH_2-C-SO_3), 53.1 (NCH_3), 64.4 (NCH_2), 66.8 (CH_2SO_3). Anal calcd. for $C_{22}H_{48}N_2O_6S_2$ (500.75): C 52.77, H 9.66, N 5.29, S 12.8; found: C 52.13, H 9.42, N 5.39, S 12.23.

Typical procedure for the synthesis of compounds 3

Sulfobetaine **3** was prepared by the addition of α,ω-bis(*N*,*N*-dimethylamino) alkane (1×10^{-2} mol) to a stirred solution of 1,3-propane sultone (2×10^{-3} mol) in anhyd acetone (50 mL). The reaction mixture was stirred at room temperature for 3 h, cooled, and filtered. The amphiphilic product was purified by recrystallization from methanol–ether (1:9), and dried in vacuo over phosphorus pentoxide.

*1-(*N,N-*dimethylammonio*-N-*propyl-1-sulfonate)-8-(*N′,N′-*dimethylamino)octane (**3a**)*

Yield: 98%. White powder, mp 198–200°C. IR (KBr) (cm^{-1}): 1480 (C-N^+), 1040 (S=0). ^1H NMR (80 MHz, D_2O) δ 1.2 (m, 12H, $(CH_2)_6$), 2.0–2.2 (m, 10H, NCH_2, NCH_3, CH_2-C-SO_3), 2.7–3.2 (m, 12H, N^+CH_3, N^+CH_2, $CH_2SO_3^-$). ^{13}C NMR (200 MHz, D_2O) δ 20.7–31.6 ($(CH_2)_6$), 46.5 (NCH_3), 49.8 (CH_2-C-SO_3), 53.2 (N^+CH_3), 61.4 (NCH_2), 64.5 (N^+CH_2), 66.7 ($CH_2SO_3^-$). Anal. calcd. for $C_{15}H_{34}N_2O_3S$ (322.5): C 55.86, H 10.63, N 8.69, S 9.94; found: C 55.50, H 10.46, N 8.46, S 9.62.

*1-(*N,N-*dimethylammonio*-N-*propyl-1-sulfonate)-12-(*N′,N′-*dimethylamino)dodecane (**3b**)*

Yield: 98%. White powder, mp 230°C. IR (KBr) (cm^{-1}): 1480 (C-N^+), 1040 (S=0). ^1H NMR (80 MHz, D_2O) δ 1.2 (m, 20H, $(CH_2)_{10}$), 1.9–2.2 (m, 10H, NCH_2, NCH_3, CH_2-C-SO_3^-), 2.9–3.2 (m, 12H, N^+CH_3, N^+CH_2, CH_2-$CH_2SO_3^-$). ^{13}C NMR (200 MHz, D_2O) δ 20.7–31.6 ($(CH_2)_{10}$), 46.5 (NCH_3), 49.8 (CH_2-C-SO_3), 53.2 (N^+CH_3), 61.4 (NCH_2), 64.5 (N^+CH_2), 66.7 ($CH_2SO_3^-$). Anal. calcd. for $C_{19}H_{49}N_2O_3S$ (378.61): C 60.27, H 11.18, N 7.40, S 8.47; found: C 59.93, H 11.02, N 7.07, S 8.54.

Typical procedure for the synthesis of compounds 4

A mixture of sulfobetaine **3** (1×10^{-2} mol) and of haloalkane (1×10^{-2} mol) in absolute MeOH (50 mL) was heated at reflux for 4 h. After removing the solvent in vacuo, the residual oil was purified by trituration with anhyd ether, and then evaporated in vacuo and dried over phophorus pentoxide.

*1-(*N,N-*dimethylammonio*-N-*propyl-1-sulfonate)-8-(*N′-*trimethylammonium iodid)octane* ***(4a)***

Yield: 95%. Yellow powder, mp 225°C. IR (KBr) (cm^{-1}): 1480 (C-N^+), 1040 (S=0). ^1H NMR (80 MHz, D_2O) δ 1.2 (m, 12H, $(CH_2)_6$), 2.1 (qt, 2H, CH_2-C-SO_3^-), 3.0–3.5 (m, 23H, NCH_3, NCH_2, $CH_2SO_3^-$). ^{13}C NMR (200 MHz, D_2O) δ 20.0–31.0 ($(CH_2)_6$), 49.9 (CH_2-C-SO_3), 53.2 and 55.5 (NCH_3), 66.3 ($NCH_2(SO_3)$), 66.7 ($CH_2SO_3^-$), 69.4 ($NCH_2(I)$). Anal. calcd. for $C_{16}H_{37}IN_2O_3S$ (464.45): C 41.38, H 8.03, N 6.03, S 6.91; found: C 40.93, H 8.34, N 5.95, S 6.95.

*1-(*N,N-*dimethylammonio*-N-*propyl-1-sulfonate)-12-(*N′-*trimethylammonium iodid)dodecane* ***(4b)***

Yield: 95%. Yellow powder, mp 222°C. IR (KBr) (cm^{-1}): 1480 (C-N^+), 1040 (S=0). ^1H NMR (80 MHz, D_2O) δ 1.2 (m, 20H, $(CH_2)_{10}$), 2.1 (qt, 2H, CH_2-C-SO_3^-), 2.8–3.2 (m, 23H, NCH_3, NCH_2, $CH_2SO_3^-$). ^{13}C NMR (200 MHz, D_2O) δ 26.7–31.1 ($(CH_2)_{10}$), 49.8 (CH_2-C-SO_3), 53.2 and 55.3 (NCH_3), 64.4 ($NCH_2(SO_3)$), 66.7 ($CH_2SO_3^-$), 69.3 (N^+CH_2). Anal. calcd. for $C_{20}H_{45}IN_2O_3S$ (520.56), C 46.15, H 8.71, N 5.38, S 6.16; found: C 45.96, H 8.93, N 5.18, S 6.00.

*1-(*N,N-*dimethylammonio*-N-*propyl-1-sulfonate)-8-(*N′,N′-*dimethyl*-N′-*dodecylammonium bromid)octane* ***(4c)***

Yield: 87%. White powder, mp 120°C. IR (KBr) (cm^{-1}): 1480 (C-N^+), 1040 (S=0). ^1H NMR (80 MHz, D_2O) δ 0.8 (t, 3H, CH_3-C_{11}), 1.3 (m, 32H, $(CH_2)_{10}$, $(CH_2)_6$), 2.1 (qt, 2H, CH_2-C-SO_3^-), 2.6–3.3 (m, 22H, NCH_3, NCH_2, $CH_2SO_3^-$). ^{13}C NMR (200 MHz, D_2O) δ 16.6 (C-CH_3), 20.8–34.6 ($(CH_2)_6$, $(CH_2)_{10}$), 49.9 (CH_2-C-SO_3), 53.5 and 54.4 (NCH_3), 64.5 and 66.3 (NCH_2), 66.7 ($CH_2SO_3^-$), 69.4 (N^+CH_2). Anal. calcd. for $C_{27}H_{59}BrN_2O_3S{\cdot}H_2O$ (550.63): C 58.84, H 11.07, N 5.08, S 5.81; found: C 58.95, H 10.95, N 4.80, S 6.00.

*1-(*N,N-*dimethylammonio*-N-*propyl-1-sulfonate)-12-(*N′,N′-*dimethyl*-N′-*dodecylammonium bromid)dodecane* ***(4d)***

Yield: 85%. White powder, mp 105°C. IR (KBr) (cm^{-1}): 1480 (C-N^+), 1040 (S=0). ^1H NMR (80 MHz, D_2O) δ 0.8 (t, 3H, CH_3-C_{11}), 1.3 (m, 40H, $(CH_2)_{10}$, $(CH_2)_{10}$), 2.1 (qt, 2H, CH_2-C-SO_3^-), 3.0–3.3 (m, 22H, NCH_3, NCH_2, $CH_2SO_3^-$). ^{13}C NMR (200 MHz, D_2O) δ 16.6 (C-CH_3), 20.6–34.4 ($(CH_2)_{10}$), 49.9 (CH_2-C-SO_3), 53.5 and 54.4 (NCH_3), 64.2 and 66.1 (NCH_2), 66.3 ($CH_2SO_3^-$). Anal. calcd. for $C_{31}H_{61}BrN_2O_3S{\cdot}H_2O$ (645.85): C 57.59, H 9.75, N 4.33, S 4.95; found: C 55.79, H 10.05, N 4.42, S 4.55.

*1-(*N,N-*dimethylammonio*-N-*propyl-1-sulfonate)-8-(*N′,N′-*dimethyl*-N′-*ethylammonium bromid) octane* ***(4e)***

Yield: 82%.White powder, mp 115°C. ^1H NMR (80 MHz, D_2O) δ 1.1 (t, 3H, CH_3), 1.5 (m, 12H, $(CH_2)_6$), 2.1 (qt, 2H, CH_2-C-SO_3), 2.9–3.1 (m, 14H, N-CH_3, CH_2SO_3), 3.3 (m, 8H, NCH_2), 3.5 (t, 2H, NCH_2-C-S). ^{13}C NMR (200 MHz, D_2O) δ 10.13 (CH_3), 21.0–31.0 $(CH_2)_6$, 47.8 (CH_2-C-S), 52.4 (NCH_3), 52.2 (CH_3N-S), 62.0, 63.7, 65.8 (NCH_2), 66.5 (CH_2S). Anal. calcd. for $C_{17}H_{39}BrN_2O_3S{\cdot}H_2O$ (449.49): C 45.43, H 9.19, N 6.23, S 7.13; found: C 45.62, H 9.05, N 5.98, S 7.35.

*1-(*N,N-*dimethylammonio*-N-*propyl-1-sulfonate)-12-(*N′,N′-*dimethyl*-N′-*ethylammonium bromid)dodecane* ***(4f)***

Yield: 80%.White powder, mp 125°C. ^1H NMR (80 MHz, D_2O) δ 1.1 (t, 3H, CH_3), 1.3 (m, 16H, $(CH_2)_8$), 2.2 (qt, 2H, CH_2-C-SO_3), 2.9–3.2 (m, 14H, N-CH_3, CH_2SO_3), 3.3 (m, 8H, NCH_2), 3.6 (t, 2H, NCH_2-C-S). ^{13}C NMR (200 MHz, D_2O) δ 10.03 (CH_3), 20.7–31.1 ($(CH_2)_8$), 49.8 (CH_2-C-S), 52.4 (NCH_3), 53.2 (CH_3N-S), 62.0, 64.48, 66.1 (NCH_2), 66.6 (CH_2S). Anal. calcd. for $C_{21}H_{47}BrN_2O_3S{\cdot}H_2O$ (505.60): C 49.88, H 9.77, N 5.54, S 4.08; found: C 50.02, H 9.94, N 5.28, S 4.42.

Typical procedure for the synthesis of compounds 5

A mixture of monosulfonate **3** (1×10^{-2} mol) and bromoacetate (2×10^{-2} mol) in anhyd methanol (40 mL) was heated at reflux under agitation for 6 h. The solvent was evaporated in vacuo. The residual oil was precipitated by ether and purified by washed successively with ether and acetone.

*1-(*N,N-*dimethylammonio*-N-*propyl-1-sulfonate)-8-(*N′,N′-*dimethyl*-N′-*ethylacetate ammonium bromid)octane* ***(5a)***

Yield: 88%. White powder, mp 185–190°C. IR (KBr) (cm^{-1}): 1470–1460 (C-N^+), 1040 (S=0), 1640 (C=O). ^1H NMR (80 MHz, D_2O) δ 1.3 (m, 8H, $(CH_2)_4$), 1.7 (m, 4H, CH_2-C-N), 2.1 (qt, 2H, CH_2-C-SO_3^-), 2.6–3.5 (m, 20H, NCH_3, NCH_2, $CH_2SO_3^-$), 3.8 (s, 3H, OCH_3), 4.2 (s, 2H, CH_2CO_2). ^{13}C NMR (200 MHz, D_2O) δ 20.8–34.6 ($(CH_2)_6$), 50.0 (CH_2-C-SO_3), 53.3 and 54.3 (NCH_3), 56.0 (OCH_3), 63.8 and 64.5 (NCH_2), 66.8 ($CH_2SO_3^-$), 68.5 (CH_2CO_2), 168.4 (CO_2). Anal. calcd. for $C_{18}H_{39}BrN_2O_5S$ (475.48): C 45.47, H 8.27, N 5.89, S 6.74; found: C 45.30, H 8.97, N 5.91, S 6.86.

*1-(*N,N-*dimethylammonio*-N-*propyl-1-sulfonate)-12-(*N′,N′-*dimethyl*-N′-*ethylacetate ammonium bromid)dodecane* ***(5b)***

Yield: 83%. White powder, mp 170°C. IR (KBr) (cm^{-1}): 1460 (C-N^+), 1040 (S=0), 1640 (C=O). ^1H NMR (80 MHz, D_2O) δ 1.26 (m, 16H, $(CH_2)_8$), 1.7 (m, 4H, CH_2-C-N), 2.1 (qt, 2H, CH_2-C-SO_3^-), 3.0–3.2 (m, 22H, NCH_3, NCH_2, $CH_2SO_3^-$), 3.8 (s, 3H, OCH_3), 4.2 (s, 2H, CH_2CO_2). ^{13}C NMR (200 MHz, D_2O) δ 20.8–31.2 ($(CH_2)_{10}$), 50.0 (CH_2-C-SO_3), 53.3 and 54.4 (NCH_3), 56.0 (OCH_3), 63.7 and 64.6 (NCH_2), 68.5 ($CH_2SO_3^-$), 68.7 (CH_2CO_2), 168.4 (CO_2). Anal. calcd. for $C_{22}H_{47}BrN_2O_5S$ (531.59): C 49.71, H 8.91, N 5.27, S 6.03; found: C 49.67, H 9.03, N 4.98, S 6.02.

Typical procedure for the synthesis of compounds 6

A mixture of compound **5** (1×10^{-2} mol) in methanol and anion-exchange resin (OH^-) (amberlist IRA 400) (25 g) was stirred for 3 h at room temperature. Then, the mixture was filtered and evaporated in vacuo. The residual oil was triturated from ether, and recrystallized from ether–methanol (9:1).

*1-(*N,N-*dimethylammonio*-N-*propyl-1-sulfonate)-8-(*N′,N′-*dimethylammonio*-N′-*acetate)octane* ***(6a)***

Yield: 78%. White powder, mp 230°C. IR (KBr) (cm^{-1}): 1480 (C-N^+), 1200 and 1050 (S=0), 1650–1630 (C=O). ^1H NMR (200 MHz, D_2O) δ 1.4 (m, 8H, $(CH_2)_4$), 1.8 (m, 4H, CH_2-C-N), 2.2 (qt, 2H, CH_2-C-SO_3^-), 2.9 (t, 2H, CH_2SO_3), 3.0 and 3.1 (s, 12H, NCH_3), 3.4–3.6 (m, 6H, NCH_2), 3.8 (s, 2H, CH_2CO_2). ^{13}C NMR (200 MHz, D_2O) δ 20.8–30.4 ($(CH_2)_6$), 49.9 (CH_2-C-SO_3), 53.2 and 53.9 (NCH_3), 64.5 (NCH_2), 66.8 ($CH_2SO_3^-$), 68.6 (CH_2CO_2), 171.9 (CO_2). Anal. calcd. for $C_{17}H_{36}N_2O_5S{\cdot}H_2O$ (396.54): C 51.44,

H 9.58, N 7.06, S 8.06; found: C 51.24, H 9.71, N 6.97, S 8.44.

*1-(*N,N-*dimethylammonio*-N-*propyl-1-sulfonate)-12-(*N′,N′-*dimethylammonio*-N′-*acetate)dodecane (**6b**)*

Yield: 75%. White powder, mp 260°C. IR (KBr) (cm^{-1}): 1480 (C-N^+), 1200 and 1050 (S=0), 1650–1630 (C=O). ^{1}H NMR (200 MHz, D_2O) δ 1.3 (m, 16H, $(CH_2)_8$), 1.7 (m, 4H, CH_2-C-N), 2.2 (qt, 2H, CH_2-C-SO_3^-), 2.3 (t, 2H, CH_2SO_3), 3.0 and 3.2 (s, 12H, NCH_3), 3.4–3.6 (m, 6H, NCH_2), 3.7 (s, 2H, CH_2CO_2). ^{13}C NMR (200 MHz, D_2O) δ 20.7–30.4 ($(CH_2)_{10}$), 49.8 (CH_2-C-SO_3), 53.2 and 53.8 (NCH_3), 64.4 (NCH_2), 67.1 ($CH_2SO_3^-$), 68.6 (CH_2CO_2), 171.8 (CO_2). Anal. calcd. for $C_{21}H_{44}N_2O_5S\cdot H_2O$ (454.65): C 55.43, H 10.11, N 6.15, S 7.03; found: C 55.42, H 10.43, N 5.82, S 7.28.

References

1. N. Kimizuka, T. Wakiyama, H. Miyauchi, T. Yoshimi, M. Tokuhiro, and T. Kunitake. J. Am. Chem. Soc. **118**, 5808 (1996) and refs. cited therein.
2. G.H. Escamilla. *In* Advances in dendrinic macromolecules. Vol 2. *Edited by* JAJ Press Inc. 1995. pp. 157–190.
3. J.H. Fuhrhop and J. Mathieu. J. Chem. Soc. Chem. Commun. 144 (1983).
4. S. Souirti and M. Baboulène. in press.
5. XXIX CED annual Meeting. Barcelona. 1999. May.
6. T.A. Spencer, T.J. Onofrey, R.O. Cann, J.S. Russel, L.E. Lee, D.E. Blanchard, A. Castro, P. Gu, G. Jiang, and I. Schechter. J. Org. Chem. **64**, 807 (1999).
7. E.J. Fendler, C.L. Day, and J.H. Fendler. J. Phys. Chem. **76**, 1460 (1972).
8. J.W. Gibbs. The collected works of J.W. Gibbs. Vol 1. Longmans and Green, London. 1928. p. 119.
9. F.M. Menger and S. Wreen. J. Phys. Chem. **78**, 1387 (1974).
10. S. Bhattacharya and S. De. J. Chem. Soc. Chem. Commun. 651 (1995).
11. Y. Chevalier, S. Brunel, and P. Le Perchec. J. Chim. Phys. - Chim. Biol. **92**, 1025 (1995).
12. J.B. Le Toumelin and M. Baboulène. Langmuir, **12**, 2128 (1996).
13. S. Franceschi, N. de Viguerie, M. Rivière, and A. Lattes. New. J. Chem. **23**, 447 (1999) and refs. cited therein.