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A Synthetic Route to Sulfobetaine Methacrylates with Varying Charge Distance

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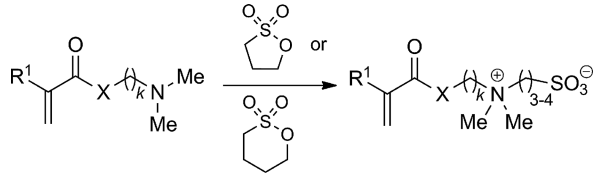
A general synthetic strategy is described that enables access to a library of new sulfobetaine methacrylates starting from commercially available precursors. The three-step procedure allows the distance between the quaternary amine and the sulfonate group (inner charge distance) to be varied by selecting the corresponding dibromoalkane in the first step. A key step is the final esterification, in which methacrylic acid acts as solvent as well as reagent for the zwitterionic hydroxy intermediates. Thus, it is possible to synthesize monomeric precursors with up to twelve methylene groups between the positive and the negative charge. A selection of these monomers has been successfully tested for their ability to polymerize using free-radical polymerization.

Introduction

Zwitterionic (macro)molecules are known for their wide spectrum of interesting properties and they are used in many different fields of applied chemistry and materials science.[1] Applications range from polar surfactants[2] and stationary phases in zwitterionic hydrophilic interaction chromatography[3] to their use as polymer brushes for surface modifications.[4] When attached to surfaces, zwitterionic polymers are utilized as antifouling materials to prevent nonspecific adsorption of proteins[5] or the adhesion of bacteria.[6] In particular, poly(sulfobetaine) coated surfaces have recently attracted attention as potential cell culture substrates because of their ability to sustain long-term growth of human embryonic stem cells.[7] Furthermore, the long-term stability of cell micropatterns on poly(sulfobetaine)-patterned surfaces was reported.[8]

Most of the applications mentioned above require zwitterionic monomers bearing polymerizable vinyl groups such as methacrylate or acrylate derivatives. Because the structure of the monomeric unit influences the properties of the corresponding polymer, the development of synthetic strategies for the preparation of new zwitterionic precursors is of great interest. In principle, sulfobetaine monomers are easily accessible through ring-opening reaction of sultones by using tertiary amines bearing polymerizable groups as nucleophiles (Scheme 1).[9] Laschewsky et al. used this general procedure to synthesize a library of sulfobetaine precursors, in which the structure of the monomer was varied by selecting a suitable nucleophile.[10] The corresponding polymers obtained by free-radical polymerization of these monomers were furthermore classified by their polymer geometry. Although this general synthetic procedure leads to a large number of different molecules, the method is limited to monomers bearing three or four methylene groups between the positive and the negative charge (inner charge distance).



Scheme 1. General synthetic route to sulfobetaine monomers via sultones; R^1 = H, CH_3. X = O, NH. k = 2–11.

Weers et al. investigated the influence of the inner charge distance on the solution properties of carboxy- and sulfobetaines. For this purpose, sulfobetaines with inner charge distances as high as six methylene groups were synthesized through the reaction of tertiary alkylamines with a large excess of dibromoalkanes and subsequent sulfonation of the remaining bromine.[11] Although this procedure does not include the introduction of polymerizable vinylic groups, in principle, it enables access to a group of sulfobetaines with varying charge separation distance.

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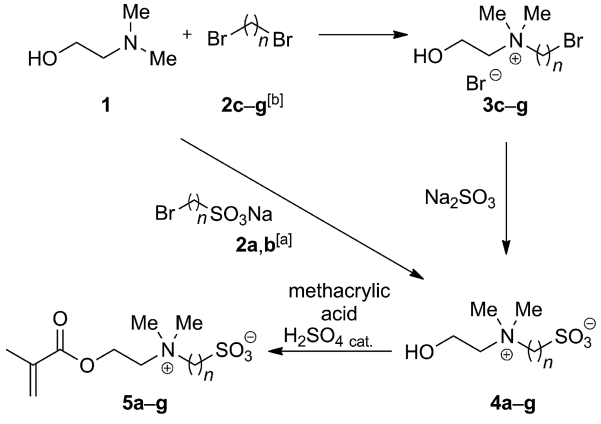
Currently, there are only a few published procedures that allow access to polymerizable sulfobetaine monomers with inner charge distances of less than three or more than four methylene groups. Terayama et al. published a procedure for the synthesis of a sulfobetaine methacrylate with only two methylene groups between the charge-bearing groups, through the reaction of 2-(dimethylamino)ethyl methacrylate with vinylsulfonyl chloride.[12] However, this specialized route is limited to only this specific inner charge distance. Sonnenschein et al. reported the synthesis of a group of styrene sulfobetaine monomers with inner charge distances ranging from one to five methylene groups, aiming to investigate the effects of the charge distances on zwitterionic ion chromatography separations. The presented sulfonates were synthesized by applying a series of nucleophilic substitution reactions (including the ring-opening reaction of sultones), whereby the synthesis protocols were chosen according to their efficacy depending on the number of methylene groups between the charges.[13] However, the described method for the monomer bearing five methylene groups through conversion of 5-bromopentane-1-sulfonate with a tertiary amine can, in theory, be adapted to the synthesis of sulfobetaines bearing more than five methylene groups between the charges.

Our work has been motivated by the need to develop a generic and efficient synthesis protocol with which to access sulfobetaine methacrylates with free control over the number of methylene groups between the charges. We present a three-step synthesis for sulfobetaine methacrylates with variably controllable inner charge distances starting from commercially available, inexpensive precursors (Scheme 2). The number of methylene groups between the two charges in the final monomer is determined by the choice of the corresponding 1,*n*-dibromoalkane, under otherwise identical conditions, underpinning the highly general character of this procedure. Thus, our approach will enable broad access to a library of new zwitterionic monomers, which represent useful building blocks for applications in different fields of biology, polymer chemistry, and materials science.



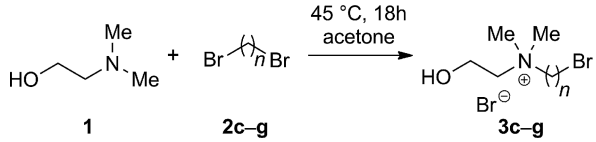
Scheme 2. Synthetic route for the variation of the inner charge distance of sulfobetaine methacrylates. [a] n = 2 and 3. [b] n = 4, 5, 6, 8, and 12.

Results and Discussion

Monomer Synthesis

Starting from commercially available 1,*n*-dibromoalkanes **2c**–**g**, the bromoalkyl quaternary bromide salts **3c**–**g** were accessible through nucleophilic substitution by using 2-(dimethylamino)ethanol (**1**) as nucleophile (Table 1).

Table 1. Formation of the bromoalkyl quaternary bromide salts (Step 1).



Entry	Starting material	*n*	Product	Yield [%]
1	1,4-dibromobutane (**2c**)	4	**3c**	62
2	1,5-dibromopentane (**2d**)	5	**3d**	76
3	1,6-dibromohexane (**2e**)	6	**3e**	75
4	1,8-dibromooctane (**2f**)	8	**3f**	80
5	1,12-dibromododecane (**2g**)	12	**3g**	84

To minimize the formation of the double-substituted side product, an excess of the dibromoalkane (fourfold) and the slow addition of the nucleophile over a period of 6 h was necessary. Given their insolubility in acetone, the small amounts of double-substituted side product could easily be removed by filtration. The main products **3c**–**g**, on the other hand, were soluble in all cases. After the reaction, the solvent was removed and a mixture of ethyl acetate and water (50:50) was added. The target compounds could be isolated from the aqueous phase and were used for the next step without further purification. The excess dibromoalkanes were recovered from the organic phase, thus making the first step highly efficient. The choice of acetone as the solvent was critically important because the direct use of ethyl acetate as solvent led, in case of **3e**, to the formation of the double-substituted compound as the main product.

The second step of the procedure included the conversion of the bromoalkyl quaternary bromide salts **3c**–**g** with sodium sulfite, leading to the corresponding sulfobetaine hydroxy intermediates **4c**–**g** (Table 2). To demonstrate the universality of our approach, we decided to expand the reaction sequence to include the synthesis of sulfobetaine methacrylates having two to twelve methylene groups (n = 2–12) between the amine and the sulfonate group. Although several of these monomers have not previously been reported, alternative, but less universal synthetic strategies exist for compounds **5a**–**c** (n = 2–4).[10,12a] Where possible, our analytical results were compared to the corresponding reported values.

In the case of compounds with n = 2 and 3, we took advantage of the fact that the bromo alkylsulfonate salts **2a** and **2b** are commercially available and were thus able to eliminate the sulfonation step of the bromoalkyl quaternary bromide salts. In fact, the conversion of **2a** and **2b** with an excess of 2-(dimethylamino)ethanol (**1**) in dimethylform-

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Table 2. Formation of the sulfobetaine alcohols (Step 2).

3c–g **4c–g**

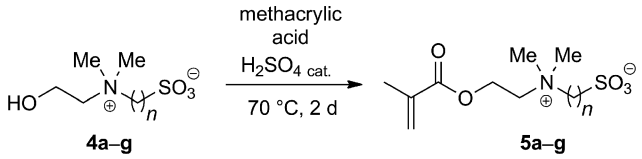
Entry	Starting material	*n*	Product	Yield [%]
1	**3c**	4	**4c**	85
2	**3d**	5	**4d**	77
3	**3e**	6	**4e**	78
4	**3f**	8	**4f**	80
5	**3g**	12	**4g**	72

amide directly resulted in the formation of sulfobetaine alcohols **4a** and **4b**. The products precipitated during the reaction and were subsequently collected by filtration. Further purification steps were not necessary. In case of compounds with $n > 3$, sulfonation of the quaternary bromide salts **3c**–**g** with sodium sulfite in aqueous solution at 90 °C for 24 h led to the formation of sulfobetaine alcohols **4c**–**g** in good yields. After removal of the solvent, the major part of unreacted starting material could be removed by dissolving the crude products in small amounts of methanol und subsequent precipitation in acetone. However, further purification of the products **4c**–**g** by means of column chromatography through a short column (silica, 10 cm) using methanol as eluent was required. Even very small amounts of the remaining starting materials **3c**–**g** in the corresponding products resulted in spontaneous polymerization of the methacrylic acid in the final esterification step.

It should be noted at this point that alternative synthetic routes to the described sulfobetaine methacrylates tested in our laboratories have proven to be less favorable. The conversion of the 1,*n*-dibromoalkanes **2c**–**g** with 2-(dimethylamino)ethyl methacrylate in a similar manner to Step 1, followed by sulfonation of the obtained quaternary bromide salts would make this route a general, two-step procedure. Tested for $n = 6$, we found that the first step is simple to perform, but unfortunately the final sulfonation resulted in an attack of the double bond by the sulfite ion. In addition, we tested the monosulfonation of 1,*n*-dibromoalkanes for $n > 4$ according to a procedure published by Fujii and Cook,[14] aiming for a further conversion of the obtained bromoalkylsulfonates with 2-(dimethylamino)ethanol (**1**) in the manner described above. Unfortunately, we were not able to isolate the monosubstituted products in acceptable yields.

The key step in the presented synthetic route is the final acid-catalyzed esterification of the obtained sulfobetaine alcohols **4a**–**g** with methacrylic acid, leading to the corresponding target compounds **5a**–**g** (Table 3). The special feature of this step lies in the fact that methacrylic acid acts as solvent as well as esterification reagent for the extremely polar, and otherwise difficult to dissolve, sulfobetaine hydroxy intermediates. Due to the poor solubility of the sulfobetaine alcohols in commonly used organic solvents, all attempts to synthesize the target compounds through alternative approaches failed, including the reaction with methacryloyl chloride or the use of coupling reagent strategies such as *N*,*N*-dicyclohexylcarbodiimide (DCC)/4-(dimethylamino)pyridine (DMAP).

Table 3. Formation of the sulfobetaine methacrylates (Step 3).



4a–g **5a–g**

Entry	Starting material	*n*	Product	Yield [%]
1	**4a**	2	**5a**	42
2	**4b**	3	**5b**	62
3	**4c**	4	**5c**	72
4	**4d**	5	**5d**	70
5	**4e**	6	**5e**	68
6	**4f**	8	**5f**	74
7	**4g**	12	**5g**	71

However, we found that methacrylic acid is able to dissolve hydroxy intermediates **4a**–**g** and simultaneous undergo an esterification reaction after adding catalytic amounts of sulfuric acid, leading to the target compounds **5a**–**g** in high yields of up to 74%. In case of **5a**, the maximum yield achieved was 42%, probably because of the poorer solubility of the starting material **4a** in methacrylic acid compared to the other starting compounds. In general, longer reaction times did not result in higher yields in all cases. To prevent spontaneous and uncontrolled polymerization of the methacrylic acid and the formed sulfobetaine methacrylates, small amounts of hydroquinone were added to the reaction mixture. Although the polarity of the hydroxy intermediates **4a**–**g** and their corresponding products **5a**–**g** are comparable, separation of the molecules by means of classic column chromatography was easily conducted by using mixtures of methanol and dichloromethane as eluent. Monomers **5a**–**g** are hygroscopic powders that quickly adsorb water in air. Indeed, elemental analysis (C, H, N, S) of the final products indicate the presence of water. In general, the measured values for C, N, and S were slightly lower, whereas the values for H were slightly higher than the theoretical values. Taking into account the adsorption of about one molecule of water per monomer, the obtained values were satisfactory.

The successful isolation of the sulfobetaine methacrylate **5g** in good yields (also in the previous reaction steps) indicates the applicability of our approach to the synthesis of sulfobetaine methacrylates bearing a larger number of methylene groups between the two charges.

Polymerization

The isolated sulfobetaine methacrylates are particularly interesting as monomeric precursors in fields of polymer chemistry and materials science; however, applications in these fields presupposes polymerizability of the vinyl group.

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Hence, the synthetic value of our new approach was demonstrated by conventional free-radical polymerization of the obtained sulfobetaine methacrylates. It should be mentioned that known compounds **5a**–**c**, which were synthesized through alternative routes, have already been successfully applied in controlled radical polymerizations.[5a,5b,12a,15]

To demonstrate the polymerizability of the obtained monomers, we subjected compounds **5a**–**g** to conditions typically used in conventional free-radical polymerizations. Polymerizations were performed in 0.5 M aqueous sodium bromide solution at 70 °C for 150 min. using 2 mol-% 4,4′-azobis(4-cyanopentanoic acid) as initiator. Monomer **5g** had to be polymerized in methanol because of its poor solubility in water. The obtained polyzwitterions were purified by dialysis against demineralized water and were furthermore analyzed by size-exclusion chromatography (see the Supporting Information 1.4). Conversions were determined by ^{1}H NMR spectroscopic analysis of the reaction solution.

As expected from conventional free-radical polymerizations, the obtained polymers **6a**–**f** showed a broad molecular weight distribution and, therefore, high polydispersities (Table 4).

Table 4. Free-radical polymerization of the sulfobetaines.

Entry	Monomer	Polymer	M_n [g/mol][a][b]	M_w [g/mol][a][c]	PDI[a][d]
1	**5a**	**6a**	67400	421300	6.30
2	**5b**	**6b**	108300	510300	4.70
3	**5c**	**6c**	116900	504000	4.30
4	**5d**	**6d**	61700	533900	8.70
5	**5e**	**6e**	95700	618600	6.50
6	**5f**	**6f**	22700	333900	14.7
7	**5g**	**6g**	n.a.	n.a.	n.a.

[a] Determined by size-exclusion chromatography. The SEC system was calibrated against PEO standards with molecular weights (M_p) ranging from 232 to 1,015,000 g mol^{-1}. [b] Number average molecular weight. [c] Weight average molecular weight. [d] M_w/M_n.

After the reaction, no monomer was detected in the ^{1}H NMR spectra of **6a**–**f** and, therefore, the yields were assumed to be quantitative. An interesting exception was found in the case of polymer **6g**, which precipitated from the reaction mixture after 15 min reaction time. Surprisingly, the obtained substance was insoluble in all commonly used organic solvents (1,4-dioxane, dimethyl sulfoxide (DMSO), CH_2Cl_2, ethanol, methanol, isopropyl alcohol (IPA), tetrahydrofuran (THF), diethyl ether, acetone, ethyl acetate, hexane) as well as water and aqueous sodium bromide solution. Therefore, neither size-exclusion chromatography nor NMR spectroscopic analysis could be conducted. Elemental analysis and IR spectrum of polymer **6g** did not show any indication of a degradation reaction. The IR spectrum of polymer **6g** revealed characteristic bands at 1168 and 1036 cm^{-1}, representing asymmetric and symmetric SO_3 stretching, as well as a band at 1716 cm^{-1}, indicative of the carbonyl group. It also shows broadened bands compared to the IR spectrum of its monomer **5g** (see the Supporting Information 1.3). The amounts of carbon, hydrogen, nitrogen, and sulfur measured by elemental analysis of polymer **6g** are close to the calculated theoretical values, but also indicate the adsorption of water [elemental analysis calcd. (%) for **6g**: C 59.23, H 9.69, N 3.45, S 7.91; found C 55.01, H 9.94, N 3.05, S 7.20]. In addition, the broad band at 3422 cm^{-1} in the IR spectrum of **6g** indicated water adsorption. Poly(sulfobetaines) are known to quickly absorb up to one molecule of water per betain unit in air because of their hygroscopic character.[10] The ^{1}H NMR spectrum of the reaction solution showed the presence of monomer **5g** only. In this study, we were mainly focused on the development of the synthetic route, therefore no further attempts at optimizing the polymerization conditions for **5g** were undertaken. Future steps will involve extensive studies that focus on the polymerization and application of the described new sulfobetaine methacrylates.

Conclusions

We report a generic synthetic strategy for the systematic preparation of a range of new sulfobetaine methacrylates in good yields. The facile, three-step procedure allows for the variation of the number of methylene groups between the positive and the negative charge in the target compound by suitable choice of the corresponding dibromoalkane in the first step, under otherwise identical conditions. A special feature of our approach is the final esterification of the extremely polar sulfobetaine hydroxy intermediates, in which methacrylic acid acts as solvent as well as esterification reagent. The universal nature of this new approach has been demonstrated by synthesizing a series of sulfobetaine methacrylates bearing two to twelve methylene groups between the charges, from which the methacrylates bearing more than four methylene groups (**5d**–**g**) have not previously been reported. Furthermore, the synthetic value of the procedure was demonstrated by conducting conventional free-radical polymerization of the obtained monomers.

Although the applicability of the presented synthetic strategy has only been tested for the maximum number of twelve methylene groups between the two charges, the results indicate broad applicability for the synthesis of sulfobetaines. In addition, structural changes of the amino alcohol nucleophile in the first step (e.g., a larger number of carbon atoms between the O and the N atom) should be compatible with the developed method. In general, our synthetic strategy enables access to a library of new sulfobetaine methacrylates that are characterized by a wide range of structural diversity. Controlled radical polymerizations of the described new monomers, especially surface-initiated ATRP and RAFT polymerizations, are being performed and the biological and physical properties of the resulting polymers are under investigation in our laboratories.

Experimental Section

General Procedure A. Typical Procedure for the Formation of Bromoalkyl Quaternary Bromide Salts 3c–g (Table 1): In a 100 mL

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two-neck flask, the corresponding 1,*n*-dibromoalkane **2c**–**g** (0.06 mol, 4.00 equiv.) was dissolved in acetone (60 mL) and heated to 45 °C. Then, 2-(dimethylamino)ethanol (**1**; 0.015 mol, 1.00 equiv.) was added slowly to this mixture over a period of 6 h, while stirring. The reaction mixture was then stirred for 18 h at 45 °C. After cooling to room temp., the white precipitation (double alcohol) was removed by filtration. The liquid phase was evaporated to remove the solvent and the oily residue was diluted with ethyl acetate (150 mL). The product was extracted with water (3× 100 mL) and the excess of the 1,*n*-dibromoalkane was recovered from the organic phase. The aqueous phases were combined and evaporated to give the corresponding bromoalkyl quaternary bromide salt **3c**–**g** as a yellowish oil.

General Procedure B. Typical Procedure for the Formation of Sulfobetaine Alcohols 4a–b: In a 250 mL flask, the corresponding sodium bromoalkylsulfonate **2a**–**b** (25.0 mmol, 1.00 equiv.) was suspended in dimethylformamide (70 mL) and heated to 70 °C. After 30 min, 2-(dimethylamino)ethanol (**1**; 100 mmol, 4.00 equiv.) was added and the mixture was stirred for 48 h at 70 °C. After cooling to room temp., the precipitated product was filtered off and washed with dimethylformamide (3× 50 mL) and diethyl ether (3× 50 mL). The product was dried in high vacuum for 3 h to give the corresponding sulfobetaine alcohol **4a**–**b** as a white solid.

General Procedure C. Typical Procedure for the Formation of Sulfobetaine Alcohols 4c–g (Table 2): In a 50 mL two-neck flask equipped with a reflux condenser, the corresponding bromoalkyl quaternary bromide salt **3c**–**g** (8.00 mmol, 1.00 equiv.) was dissolved in water (25 mL) and heated to reflux. After 10 min, sodium sulfite (9.84 mmol, 1.24 equiv.) was added to this solution and the reaction mixture was stirred and heated to reflux for 24 h. After cooling to room temp., the solvent was removed under reduced pressure and the white residue was dissolved in methanol (100 mL) and the insoluble residue was filtered off. The solvent was concentrated to 5–10 mL under reduced pressure and the product was precipitated in acetone (150 mL). The product was collected by filtration, dried in high vacuum, absorbed on silica and subjected to flash chromatography through a short column (10 cm silica; methanol) to give the corresponding sulfobetaine alcohol **4c**–**g** as a white solid.

General Procedure D. Typical Procedure for the Formation of Sulfobetaine Methacrylates 5a–g (Table 3): An oven-dried 50 mL two-neck flask fitted with a reflux condenser was evacuated and backfilled with argon and charged with the corresponding sulfobetaine alcohol **4a**–**g** (6.00 mmol) and hydroquinone (10 mg). Then methacrylic acid (30 mL) was added and the mixture was heated to 70 °C while stirring. After 30 min, sulfuric acid (5 drops) was added to this suspension and the reaction mixture was stirred for 48 h at 70 °C. After cooling to room temp., the liquid phase was separated from the brown oily phase by decantation. The oily residue was subsequently dried in vacuo, and the liquid phase was evaporated until dry. Both residues were dissolved in methanol, combined, absorbed on silica, and subjected to flash chromatography (silica; dichloromethane/methanol, 1:1) to give the corresponding sulfobetaine methacrylate **5a**–**g** as a white solid.

Polymerization: Polymers of the described zwitterionic methacrylates were obtained by radical polymerization in degassed (freeze-pump-thaw technique, 3 cycles) aqueous solutions (0.7 M monomer, 0.5 M sodium bromide) at 70 °C for 150 min, using 2 mol-% 4,4′-azobis(4-cyanopentanoic acid) (V 501) as initiator. Monomer **5g** was polymerized in methanol (0.2 M monomer) because of its poor solubility in aqueous solution. Polymers were purified by dialysis against demineralized water for 7 d using a dialysis tubing cellulose membrane (Sigma–Aldrich, cut-off 14000 Da) and were subsequently dried by freeze-drying. The obtained polymers were analyzed by size-exclusion chromatography (SEC) with 0.5 M aqueous NaBr solution/acetonitrile (80:20) (see the Supporting Information).

4-Bromo-*N*-(2-hydroxyethyl)-*N*,*N*-dimethylbutane-1-ammonium Bromide (3c): The reaction was carried out starting from 1,4-dibromobutane (**2c**) following General Procedure A, yield 2.83 g (9.28 mmol, 62%); R_f = 0.05 (methanol). ^{1}H NMR (500 MHz, MeOD): δ = 4.00 (ddd, J = 7.64, 5.28, 2.75 Hz, 2 H, OCH_2), 3.54 (t, J = 6.21 Hz, 2 H, $BrCH_2$), 3.50–3.48 (m, 2 H, NCH_3), 3.47–3.44 (m, 2 H, NCH_2), 3.18 (s, 6 H, 2×NCH_2), 2.01–1.90 (m, 4 H, CH_2) ppm. ^{13}C NMR (125 MHz, MeOD): δ = 66.71 (–, CH_2), 65.71 (–, CH_2), 56.90 (–, CH_2), 52.32 (+, 2×NCH_3), 32.98 (–, CH_2), 30.51 (–, CH_2), 22.53 (–, CH_2) ppm. FTIR (ATR): $\tilde{\nu}$ = 3262 (m), 3006 (w), 2944 (w), 1490 (m), 1460 (m), 1420 (w), 1346 (w), 1326 (w), 1278 (w), 1236 (w), 1219 (w), 1146 (w), 1093 (w), 1045 (w), 995 (m), 952 (w), 939 (w), 912 (m), 898 (m), 788 (m), 746 (w), 649 (m), 600 (m), 529 (m) cm^{-1}. MS (FAB): m/z (%) = 224.1 (100) [M – Br$^-$]$^+$, 162.1 (6), 154.1 (11), 136.1 (9). HRMS (FAB): m/z calcd. for $C_8H_{19}NOBr^+$ [M – Br$^-$]$^+$ 224.0645; found 224.0647 [M – Br$^-$]$^+$.

5-Bromo-*N*-(2-hydroxyethyl)-*N*,*N*-dimethylpentane-1-ammonium Bromide (3d): The reaction was carried out starting from 1,5-dibromopentane (**2d**) following General Procedure A, yield 3.64 g (11.4 mmol, 76%); R_f = 0.06 (methanol). ^{1}H NMR (500 MHz, MeOD): δ = 3.99 (br. s, 2 H, OCH_2), 3.51–3.42 (m, 6 H, 2×NCH_2, $BrCH_2$), 3.18 (s, 6 H, 2×NCH_3), 1.98–1.92 (m, 2 H, CH_2), 1.88–1.81 (m, 2 H, CH_2), 1.56–1.50 (m, 2 H, CH_2) ppm. ^{13}C NMR (125 MHz, MeOD): δ = 66.58 (–, CH_2), 66.56 (–, CH_2), 56.30 (–, CH_2), 52.30 (+, 2×NCH_3), 33.86 (–, CH_2), 33.26 (–, CH_2), 25.98 (–, CH_2), 22.89 (–, CH_2) ppm. FTIR (ATR): $\tilde{\nu}$ = 3292 (w), 3011 (w), 2942 (w), 1628 (vw), 1465 (w), 1295 (vw), 1252 (w), 1226 (w), 1079 (w), 1008 (w), 968 (w), 921 (w), 736 (w), 639 (w), 556 (w) cm^{-1}. MS (FAB): m/z (%) = 238.1 (100) [M – Br$^-$]$^+$, 176.2 (10), 158.2 (10). HRMS (FAB): m/z calcd. for $C_9H_{21}NOBr^+$ [M – Br$^-$]$^+$ 238.0801; found 238.0800 [M – Br$^-$]$^+$.

6-Bromo-*N*-(2-hydroxyethyl)-*N*,*N*-dimethylhexane-1-ammonium Bromide (3e): The reaction was carried out starting from 1,6-dibromohexane (**2e**) following General Procedure A, yield 3.75 g (11.3 mmol, 75%); R_f = 0.09 (methanol). ^{1}H NMR (500 MHz, MeOD): δ = 4.01–3.98 (m, 2 H, OCH_2), 3.49–3.46 (m, 4 H, NCH_2, $BrCH_2$), 3.44–3.40 (m, 2 H, NCH_2), 3.17 (s, 6 H, 2×NCH_3), 1.93–1.87 (m, 2 H, CH_2), 1.86–1.79 (m, 2 H, CH_2), 1.59–1.53 (m, 2 H, CH_2), 1.45–1.38 (m, 2 H, CH_2) ppm. ^{13}C NMR (125 MHz, MeOD): δ = 66.70 (–, CH_2), 66.59 (–, CH_2), 56.92 (–, CH_2), 52.26 (+, 2×NCH_3), 34.15 (–, CH_2), 33.64 (–, CH_2), 28.68 (–, CH_2), 26.54 (–, CH_2), 23.55 (–, CH_2) ppm. FTIR (ATR): $\tilde{\nu}$ = 3288 (w), 2932 (w), 2859 (w), 1463 (w), 1249 (w), 1081 (w), 1052 (w), 1010 (w), 968 (w), 924 (w), 731 (w), 637 (w), 555 (w) cm^{-1}. MS (FAB): m/z (%) = 252.2 (100) [M – Br$^-$]$^+$, 190.0 (7), 172.5 (12). HRMS (FAB): m/z calcd. for $C_{10}H_{23}NOBr^+$ [M – Br$^-$]$^+$ 252.0963; found 252.0966 [M – Br$^-$]$^+$.

8-Bromo-*N*-(2-hydroxyethyl)-*N*,*N*-dimethyloctane-1-ammonium Bromide (3f): The reaction was carried out starting from 1,8-dibromooctane (**2f**) following General Procedure A, yield 4.34 g (12.0 mmol, 80%); R_f = 0.09 (methanol). ^{1}H NMR (500 MHz, MeOD): δ = 3.99 (br. s, 2 H, OCH_2), 3.50–3.39 (m, 6 H, 2×NCH_2, $BrCH_2$), 3.16 (s, 6 H, 2×NCH_3), 1.89–1.77 (m, 4 H, CH_2), 1.50–1.35 (m, 8 H, 4×CH_2) ppm. ^{13}C NMR (125 MHz, MeOD): δ = 66.83 (–, CH_2), 66.55 (–, CH_2), 56.92 (–, CH_2), 52.23 (+, 2×NCH_3), 34.46 (–, CH_2), 33.93 (–, CH_2), 30.05 (–, CH_2), 29.61

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(–, CH_2), 29.04 (–, CH_2), 27.31 (–, CH_2), 23.63 (–, CH_2) ppm. FTIR (ATR): $\tilde{\nu}$ = 3295 (w), 2926 (w), 2854 (w), 1628 (vw), 1463 (w), 1256 (vw), 1081 (w), 1051 (w), 964 (w), 724 (vw), 637 (w), 556 (w) cm^{-1}. MS (FAB): *m/z* (%) = 280.2 (100) $[M - Br^-]^+$, 232.2 (14), 218.2 (14), 200.2 (25), 88.1 (10). HRMS (FAB): *m/z* calcd. for $C_{12}H_{27}NOBr^+$ $[M - Br^-]^+$ 280.1271; found 280.1269 $[M - Br^-]^+$.

12-Bromo-*N*-(2-hydroxyethyl)-*N*,*N*-dimethyldodecane-1-ammonium Bromide (3g): The reaction was carried out starting from 1,12-dibromododecane (**2g**) following General Procedure A, yield 5.26 g (12.6 mmol, 84%); R_f = 0.08 (methanol). ^1H NMR (500 MHz, MeOD): δ = 4.00–3.97 (m, 2 H, OCH_2), 3.49–3.38 (m, 6 H, 2 × NCH_2, $BrCH_2$), 3.16 (s, 6 H, 2 × NCH_3), 1.87–1.76 (m, 4 H, 2 × CH_2), 1.46–1.33 (m, 16 H, 8 × CH_2) ppm. ^{13}C NMR (125 MHz, MeOD): δ = 66.87 (–, CH_2), 66.55 (–, CH_2), 56.92 (–, CH_2), 52.22 (+, 2 × NCH_3), 34.50 (–, CH_2), 34.04 (–, CH_2), 30.63 (–, CH_2), 30.61 (–, 2 × CH_2), 30.56 (–, CH_2), 30.25 (–, CH_2), 29.88 (–, CH_2), 29.20 (–, CH_2), 27.45 (–, CH_2), 23.69 (–, CH_2) ppm. FTIR (ATR): $\tilde{\nu}$ = 3235 (m), 3021 (w), 2913 (m), 2847 (m), 1738 (vw), 1462 (m), 1374 (w), 1268 (w), 1208 (w), 1091 (m), 1071 (w), 1043 (w), 1008 (w), 981 (w), 981 (w), 962 (m), 885 (w), 855 (w), 828 (vw), 759 (vw), 726 (w), 653 (w), 604 (w), 547 (w), 514 (w), 489 (w), 450 (w) cm^{-1}. MS (FAB): *m/z* (%) = 336.2 (100) $[M - Br^-]^+$, 256.2 (10), 88.0 (7). HRMS (FAB): *m/z* calcd. for $C_{16}H_{35}NOBr^+$ $[M - Br^-]^+$ 336.1897; found 336.1898 $[M - Br^-]^+$.

2-[(2-Hydroxyethyl)dimethylammonio]ethanesulfonate (4a): The reaction was carried out starting from sodium 2-bromoethanesulfonate (**2a**) following General Procedure B, yield 2.21 g (11.2 mmol, 45%); R_f = 0.18 (methanol). ^1H NMR (500 MHz, D_2O): δ = 4.09–4.06 (m, 2 H, OCH_2), 3.82–3.79 (m, 2 H, CH_2), 3.57–3.55 (m, CH_2), 3.48–3.45 (m, CH_2), 3.22 (s, 6 H, 2 × NCH_3) ppm. ^{13}C NMR (125 MHz, D_2O): δ = 66.48 (–, CH_2), 60.24 (–, CH_2), 55.36 (–, CH_2), 51.75 (+, 2 × NCH_3), 44.25 (–, CH_2) ppm. FTIR (ATR): $\tilde{\nu}$ = 3383 (w), 3250 (w), 1672 (w), 1494 (vw), 1466 (w), 1367 (vw), 1286 (vw), 1181 (m), 1094 (w), 1037 (m), 1001 (w), 936 (w), 896 (vw), 803 (w), 773 (w), 720 (w), 661 (w), 606 (w), 546 (w), 504 (w), 457 (w) cm^{-1}. MS (FAB): *m/z* (%) = 198.1 (100) $[M + H]^+$, 155.0 (10), 154.0 (35), 136.0 (24), 107.0 (7).

3-[(2-Hydroxyethyl)dimethylammonio]propane-1-sulfonate (4b): The reaction was carried out starting from sodium 2-bromopropane-1-sulfonate (**2b**) and following General Procedure B, yield 4.75 g (22.5 mmol, 90%). ^1H NMR (500 MHz, D_2O): δ = 4.07–4.04 (m, 2 H, OCH_2), 3.57–3.53 (m, 4 H, 2 × CH_2), 3.18 (s, 6 H, 2 × NCH_3), 2.98 (t, *J* = 7.3 Hz, 2 H, CH_2SO_3), 2.28–2.22 (m, 2 H, OCH_2) ppm. ^{13}C NMR (125 MHz, D_2O): δ = 65.03 (–, CH_2), 63.34 (–, CH_2), 55.25 (–, CH_2), 51.36 (+, 2 × NCH_3), 47.21 (–, CH_2), 18.18 (–, CH_2) ppm. FTIR (ATR): $\tilde{\nu}$ = 3323 (w), 3025 (vw), 2928 (vw), 1475 (w), 1352 (w), 1306 (vw), 1242 (w), 1194 (m), 1171 (m), 1080 (m), 1041 (m), 963 (w), 936 (w), 900 (w), 844 (vw), 794 (w), 763 (w), 721 (w), 647 (w), 598 (m), 558 (w), 523 (m), 504 (w), 451 (w) cm^{-1}. MS (FAB): *m/z* (%) = 212.1 (24) $[M + H]^+$, 154.1 (100) [3NBA], 137.1 (65), 136.1 (58), 120.1 (8), 107.1 (14), 89.1 (11). HRMS (FAB): *m/z* calcd. for $C_7H_{18}NO_4S$ $[M + H]^+$ 212.0949; found 212.0951.

4-[(2-Hydroxyethyl)dimethylammonio]butane-1-sulfonate (4c): The reaction was carried out starting from 4-bromo-*N*-(2-hydroxyethyl)-*N*,*N*-dimethylbutane-1-ammonium bromide (**3c**) and following General Procedure C, yield 1.53 g (6.79 mmol, 85%); R_f = 0.14 (methanol). ^1H NMR (500 MHz, MeOD): δ = 4.00 (ddd, *J* = 7.46, 5.14, 2.68 Hz, 2 H, OCH_2), 3.47–3.42 (m, 4 H, 2 × NCH_2), 3.15 (s, 6 H, 2 × NCH_3), 2.88 (t, *J* = 7.19 Hz, 2 H, CH_2SO_3), 2.02–1.95 (m, 2 H, CH_2), 1.83 (q, *J* = 7.46, 7.45 Hz, 2 H, CH_2) ppm. ^{13}C NMR (125 MHz, MeOD): δ = 66.63 (–, CH_2), 66.26 (–, CH_2), 56.90 (–, CH_2), 52.27 (+, 2 × NCH_3), 51.23 (–, CH_2), 23.00 (–, CH_2), 22.40 (–, CH_2) ppm. FTIR (ATR): $\tilde{\nu}$ = 3310 (m), 2931 (w), 1712 (vw), 1485 (w), 1420 (w), 1384 (vw), 1341 (w), 1309 (w), 1193 (m), 1160 (s), 1093 (m), 1074 (m), 1035 (s), 971 (m), 958 (m), 908 (w), 856 (m), 790 (m), 744 (w), 603 (s), 540 (m), 522 (m), 403 (m) cm^{-1}. MS (FAB): *m/z* (%) = 226.1 (100) $[M + H]^+$, 154.1 (11), 136.1 (9). HRMS (FAB): *m/z* calcd. for $C_8H_{20}NO_4S$ $[M + H]^+$ 226.1108; found 226.1105.

5-[(2-Hydroxyethyl)dimethylammonio]pentane-1-sulfonate (4d): The reaction was carried out starting from 5-bromo-*N*-(2-hydroxyethyl)-*N*,*N*-dimethylpentane-1-ammonium bromide (**3d**) and following General Procedure C, yield 1.47 g (6.16 mmol, 77%); R_f = 0.13 (methanol). ^1H NMR (500 MHz, MeOD): δ = 4.00–3.97 (m, 2 H, OCH_2), 3.47–3.45 (m, 2 H, NCH_2), 3.42–3.39 (m, 2 H, NCH_2), 3.16 (s, 6 H, 2 × NCH_3), 2.85–2.82 (m, 2 H, CH_2SO_3), 1.89–1.80 (m, 4 H, 2 × CH_2), 1.55–1.49 (m, 2 H, CH_2) ppm. ^{13}C NMR (125 MHz, MeOD): δ = 66.56 (–, CH_2), 66.54 (–, CH_2), 56.90 (–, CH_2), 52.23 (+, NCH_3), 52.20 (+, NCH_3), 51.98 (–, CH_2), 26.28 (–, CH_2), 25.47 (–, CH_2), 23.20 (–, CH_2) ppm. FTIR (ATR): $\tilde{\nu}$ = 3291 (w), 3032 (vw), 2936 (w), 2852 (w), 1465 (w), 1203 (m), 1159 (s), 1082 (m), 1030 (s), 975 (w), 946 (w), 926 (w), 887 (w), 794 (w), 685 (w), 604 (m), 535 (m), 524 (m) cm^{-1}. MS (FAB): *m/z* (%) = 240.1 (100) $[M + H]^+$, 158.2 (11), 88.1 (7). HRMS (FAB): *m/z* calcd. for $C_9H_{22}NO_4S$ $[M + H]^+$ 240.1264; found 240.1265.

6-[(2-Hydroxyethyl)dimethylammonio]hexane-1-sulfonate (4e): The reaction was carried out starting from 6-bromo-*N*-(2-hydroxyethyl)-*N*,*N*-dimethylhexane-1-ammonium bromide (**3e**) and following General Procedure C, yield 1.58 g (6.24 mmol, 78%); R_f = 0.15 (methanol). ^1H NMR (500 MHz, MeOD): δ = 4.00–3.97 (m, 2 H, OCH_2), 3.47–3.45 (m, 2 H, NCH_2), 3.42–3.38 (m, 2 H, NCH_2), 3.15 (s, 6 H, 2 × NCH_3), 2.82–2.79 (m, 2 H, CH_2SO_3), 1.85–1.78 (m, 4 H, 2 × CH_2), 1.57–1.51 (m, 2 H, CH_2), 1.45–1.39 (m, 2 H, CH_2) ppm. ^{13}C NMR (125 MHz, MeOD): δ = 66.68 (–, CH_2), 66.55 (–, CH_2), 56.91 (–, CH_2), 52.27 (–, CH_2), 52.20 (+, NCH_3), 52.18 (+, NCH_3), 28.84 (–, CH_2), 26.78 (–, CH_2), 25.58 (–, CH_2), 23.18 (–, CH_2) ppm. FTIR (ATR): $\tilde{\nu}$ = 3299 (w), 2927 (w), 2861 (w), 1483 (w), 1467 (w), 1202 (m), 1162 (m), 1081 (w), 1034 (m), 975 (w), 930 (w), 907 (w), 775 (w), 649 (w), 605 (m), 571 (w), 536 (w), 523 (m) cm^{-1}. MS (FAB): *m/z* (%) = 254.5 (100) $[M + H]^+$, 132.3 (40). HRMS (FAB): *m/z* calcd. for $C_{10}H_{24}NO_4S$ $[M + H]^+$ 254.1426; found 254.142.

8-[(2-Hydroxyethyl)dimethylammonio]octane-1-sulfonate (4f): The reaction was carried out starting from 8-bromo-*N*-(2-hydroxyethyl)-*N*,*N*-dimethyloctane-1-ammonium bromide (**3f**) and following General Procedure C, yield 1.80 g (6.40 mmol, 80%); R_f = 0.15 (methanol). ^1H NMR (500 MHz, MeOD): δ = 3.98 (br. s, 2 H, OCH_2), 3.47–3.45 (m, 2 H, NCH_2), 3.41–3.37 (m, 2 H, NCH_2), 3.15 (s, 6 H, 2 × NCH_3), 2.80–2.77 (m, 2 H, CH_2SO_3), 1.84–1.76 (m, 4 H, 2 × CH_2), 1.49–1.35 (m, 4 H, 2 × CH_2) ppm. ^{13}C NMR (125 MHz, MeOD): δ = 66.80 (–, CH_2), 66.51 (–, CH_2), 56.92 (–, CH_2), 52.57 (–, CH_2), 52.20 (+, 2 × NCH_3), 29.84 (–, CH_2), 29.69 (–, CH_2), 29.40 (–, CH_2), 27.16 (–, CH_2), 25.86 (–, CH_2), 23.47 (–, CH_2) ppm. FTIR (ATR): $\tilde{\nu}$ = 3298 (w), 3031 (vw), 2925 (w), 2845 (vw), 1613 (vw), 1474 (w), 1288 (vw), 1194 (w), 1163 (m), 1092 (w), 1031 (m), 973 (w), 943 (w), 914 (w), 856 (vw), 783 (w), 754 (vw), 725 (vw), 589 (w), 544 (w), 520 (w), 439 (vw), 410 (m) cm^{-1}. MS (FAB): *m/z* (%) = 282.2 (100) $[M + H]^+$, 200.2 (9), 154.1 (31), 136.1 (22), 107.1 (9), 81.1 (9). HRMS (FAB): *m/z* calcd. for $C_{12}H_{28}NO_4S$ $[M + H]^+$ 282.1734; found 282.1733.

12-[(2-Hydroxyethyl)dimethylammonio]dodecane-1-sulfonate (4g): The reaction was carried out starting from 12-bromo-*N*-(2-hydroxyethyl)-*N*,*N*-dimethyldodecane-1-ammonium bromide (**3g**)

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and following General Procedure C, yield 1.94 g (5.76 mmol, 72%); R_f = 0.14 (CH_2Cl_2/MeOH, 2:1). ^{1}H NMR (500 MHz, MeOD): δ = 4.00–3.97 (m, 2 H, OCH_2), 3.47–3.45 (m, 2 H, NCH_2), 3.41–3.38 (m, 2 H, NCH_2), 3.15 (s, 6 H, 2 × NCH_3), 2.79–2.76 (m, 2 H, CH_2SO_3), 1.83–1.75 (m, 4 H, 2 × CH_2), 1.44–1.33 (m, 16 H, 8 × CH_2) ppm. ^{13}C NMR (125 MHz, MeOD): δ = 66.87 (–, CH_2), 66.52 (–, CH_2), 56.92 (–, CH_2), 52.73 (–, CH_2), 52.19 (+, 2 × NCH_3), 30.23 (–, 2 × CH_2), 30.20 (–, CH_2), 30.08 (–, 2 × CH_2), 30.00 (–, CH_2), 29.58 (–, CH_2), 27.34 (–, CH_2), 25.89 (–, CH_2), 23.59 (–, CH_2) ppm. FTIR (ATR): $\tilde{\nu}$ = 3420 (w), 3298 (w), 2961 (vw), 2914 (w), 2846 (w), 1638 (vw), 1482 (w), 1463 (w), 1354 (vw), 1215 (w), 1171 (m), 1096 (m), 1072 (w), 1039 (m), 1004 (w), 986 (w), 970 (w), 924 (w), 791 (w), 601 (m), 540 (w), 521 (m), 450 (w) cm^{-1}. MS (FAB): *m/z* (%) = 338.2 (100) [M + H]$^+$, 256.4 (11), 154.3 (9), 89.4 (10). HRMS (FAB): *m/z* calcd. for $C_{16}H_{36}NO_4S$ [M + H]$^+$ 338.2365; found 338.2368.

2-{[2-(Methacryloyloxy)ethyl]dimethylammonio}ethanesulfonate (5a): The reaction was carried out starting from 2-[(2-hydroxyethyl)dimethylammonio]ethanesulfonate (**4a**) and following General Procedure D, yield 669 mg (2.52 mmol, 42%); R_f = 0.21 (CH_2Cl_2/MeOH, 1:1). ^{1}H NMR (500 MHz, D_2O): δ = 6.17 (s, 1 H, C=CH_2), 5.78 (s, 1 H, C=CH_2), 4.66 (br. s, 2 H, OCH_2), 3.86–3.81 (m, 4 H, 2 × NCH_2), 3.50–3.47 (m, 2 H, CH_2SO_3), 3.26 (s, 6 H, 2 × NCH_3), 1.94 (s, 3 H, H_2C=CCH_3) ppm. ^{13}C NMR (125 MHz, D_2O): δ = 168.37 (C_{quat}, C=O), 135.05 (C_{quat}, C=CH_2), 127.76 (–, C=CH_2), 63.04 (–, CH_2), 60.36 (–, CH_2), 58.30 (–, CH_2), 51.45 (+, 2 × NCH_3), 44.13 (–, CH_2), 17.25 (+, H_2C=CCH_3) ppm. FTIR (ATR): $\tilde{\nu}$ = 1705 (m), 1632 (w), 1486 (w), 1458 (w), 1319 (w), 1297 (w), 1282 (w), 1207 (m), 1189 (m), 1156 (w), 1123 (m), 1063 (w), 1037 (m), 963 (w), 940 (w), 910 (w), 819 (w), 767 (m), 652 (vw), 620 (m), 598 (m), 540 (w), 524 (m), 475 (w), 458 (w) cm^{-1}. MS (FAB): *m/z* (%) = 266.1 (100) [M + H]$^+$, 184.1 (5), 154.1 (9), 114.1 (9), 113.1 (100) [M – $C_4H_{10}NSO_3$]$^+$, 95.1 (6). HRMS (FAB): *m/z* calcd. for $C_{10}H_{20}NO_5S$ [M + H]$^+$ 266.1062; found 266.1059. $C_{10}H_{19}NO_5S$ (265.32): calcd. C 45.27, H 7.22, N 5.28, S 12.09; found C 44.19, H 7.23, N 5.20, S 11.90.

3-{[2-(Methacryloyloxy)ethyl]dimethylammonio}propane-1-sulfonate (5b): The reaction was carried out starting from 3-[(2-hydroxyethyl)dimethylammonio]propane-1-sulfonate (**4b**) and following General Procedure D, yield 1.04 g (3.72 mmol, 62%); R_f = 0.15 (CH_2Cl_2/MeOH, 1:1). ^{1}H NMR (500 MHz, D_2O): δ = 6.17 (s, 1 H, C=CH_2), 5.79 (s, 1 H, C=CH_2), 4.65 (t, *J* = 2.2 Hz, 2 H, OCH_2), 3.84–3.82 (m, 2 H, NCH_2), 3.61–3.58 (m, 2 H, NCH_2), 3.23 (s, 6 H, 2 × NCH_3), 2.98 (t, *J* = 7.3 Hz, 2 H, CH_2SO_3), 2.31–2.23 (m, 2 H, CH_2), 1.95 (s, 3 H, H_2C=CCH_3) ppm. ^{13}C NMR (125 MHz, D_2O): δ = 168.42 (C_{quat}, C=O), 135.14 (C_{quat}, C=CH_2), 127.70 (–, C=CH_2), 63.43 (–, CH_2), 62.51 (–, CH_2), 58.34 (–, CH_2), 51.25 (+, 2 × NCH_3), 47.19 (–, CH_2), 18.24 (–, CH_2), 17.25 (+, H_2C=CCH_3) ppm. IR (ATR): $\tilde{\nu}$ = 3450 (vw), 1722 (w), 1634 (vw), 1455 (vw), 1423 (vw), 1322 (vw), 1302 (w), 1215 (w), 1160 (m), 1036 (m), 957 (w), 904 (w), 817 (vw), 798 (w), 720 (vw), 601 (w), 529 (m), 457 (w) cm^{-1}. MS (FAB): *m/z* (%) = 280.2 (100) [M + H]$^+$, 217.2 (4), 176.1 (4), 166.1 (6), 136.2 (48), 113.2 (20) [M – $C_5H_{12}NSO_3$]$^+$, 107.2 (13), 89.2 (10). HRMS (FAB): *m/z* calcd. for $C_{11}H_{22}NO_5S$ [M + H]$^+$ 280.1219; found 280.1216. $C_{11}H_{21}NO_5S$ (279.35): calcd. C 47.29, H 7.58, N 5.01, S 11.48; found C 44.34, H 7.99, N 4.62, S 10.79.

4-{[2-(Methacryloyloxy)ethyl]dimethylammonio}butane-1-sulfonate (5c): The reaction was carried out starting from 4-[(2-hydroxyethyl)dimethylammonio]butane-1-sulfonate (**4c**) and following General Procedure D, yield 1.27 g (4.32 mmol, 72%); R_f = 0.13 (CH_2Cl_2/MeOH, 1:1). ^{1}H NMR (500 MHz, MeOD): δ = 6.18 (s, 1 H, C=CH_2), 5.75–5.74 (s, 1 H, C=CH_2), 4.65–4.64 (m, 2 H, OCH_2), 3.79–3.77 (m, 2 H, NCH_2), 3.50–3.47 (m, 2 H, NCH_2), 3.20 (s, 6 H, 2 × NCH_3), 2.90 (t, *J* = 7.3 Hz, 2 H, CH_2SO_3), 2.05–1.98 (m, 5 H, CH_2, C=CCH_3), 1.89–1.83 (m, 2 H, CH_2) ppm. ^{13}C NMR (125 MHz, MeOD): δ = 167.69 (C_{quat}, C=O), 137.13 (C_{quat}, C=CH_2), 127.37 (–, C=CH_2), 66.13 (–, CH_2), 64.02 (–, CH_2), 59.14 (–, OCH_2), 51.96 (+, 2 × NCH_3), 51.28 (–, CH_2), 23.02 (–, CH_2), 22.39 (–, CH_2), 18.43 (+, C=CCH_3) ppm. FTIR (ATR): $\tilde{\nu}$ = 3032 (vw), 1713 (w), 1637 (vw), 1468 (w), 1314 (w), 1184 (m), 1151 (m), 1035 (m), 929 (w), 808 (w), 723 (w), 607 (w), 537 (w), 522 (m), 404 (vw) cm^{-1}. MS (FAB): *m/z* (%) = 294.2 (94) [M + H]$^+$, 212.3 (23), 156.3 (8). 113.3 (100) [M – $C_6H_{14}NSO_3$]$^+$. HRMS (FAB): *m/z* calcd. for $C_{12}H_{24}NO_5S$ [M + H]$^+$ 294.1375; found 294.1377. $C_{12}H_{23}NO_5S$ (293.38): calcd. C 49.13, H 7.90, N 4.77, S 10.93; found C 48.76, H 7.91, N 4.61, S 10.66.

5-{[2-(Methacryloyloxy)ethyl]dimethylammonio}pentane-1-sulfonate (5d): The reaction was carried out starting from 5-[(2-hydroxyethyl)dimethylammonio]pentane-1-sulfonate (**4d**) and following General Procedure D, yield 1.29 g (4.20 mmol, 70%); R_f = 0.13 (CH_2Cl_2/MeOH, 1:1). ^{1}H NMR (500 MHz, MeOD): δ = 6.15 (s, 1 H, C=CH_2), 5.73 (m, 1 H, C=CH_2), 4.62 (br. s, 2 H, OCH_2), 3.76–3.74 (m, 2 H, NCH_2), 3.44–3.40 (m, 2 H, NCH_2), 3.18 (s, 6 H, 2 × NCH_3), 2.84–2.81 (m, 2 H, CH_2SO_3), 1.97 (s, 3 H, H_2C=CCH_3), 1.89–1.81 (m, 4 H, 2 × CH_2), 1.55–1.51 (m, 2 H, CH_2) ppm. ^{13}C NMR (125 MHz, MeOD): δ = 167.68 (C_{quat}, C=O), 137.13 (C_{quat}, C=CH_2), 127.37 (–, C=CH_2), 66.44 (–, CH_2), 63.91 (–, CH_2), 59.09 (–, CH_2), 51.94 (–, CH_2), 51.90 (+, 2 × NCH_3), 26.27 (–, CH_2), 25.49 (–, CH_2), 23.19 (–, CH_2), 18.42 (+, H_2C=CCH_3) ppm. FTIR (ATR): $\tilde{\nu}$ = 3434 (w), 2964 (vw), 1712 (m), 1638 (vw), 1469 (w), 1368 (vw), 1323 (w), 1298 (w), 1262 (vw), 1171 (s), 1034 (m), 974 (w), 952 (w), 921 (w), 902 (w), 816 (w), 787 (w), 730 (w), 654 (vw), 600 (m), 545 (w), 522 (m), 483 (w) cm^{-1}. MS (FAB): *m/z* (%) = 308.2 (100) [M + H]$^+$, 240.1 (7), 226.2 (7), 154.0 (10), 113.0 (27) [M – $C_7H_{16}NSO_3$]$^+$. HRMS (FAB): *m/z* calcd. for $C_{13}H_{26}NO_5S$ [M + H]$^+$ 308.1526; found 308.1524. $C_{13}H_{25}NO_5S$ (307.41): calcd. C 50.79, H 8.20, N 4.56, S 10.43; found C 49.43, H 8.07, N 4.33, S 10.33.

6-{[2-(Methacryloyloxy)ethyl]dimethylammonio}hexane-1-sulfonate (5e): The reaction was carried out starting from 6-[(2-hydroxyethyl)dimethylammonio]hexane-1-sulfonate (**4e**) and following General Procedure D, yield 1.31 g (4.08 mmol, 68%); R_f = 0.14 (CH_2Cl_2/MeOH, 1:1). ^{1}H NMR (500 MHz, MeOD): δ = 6.16–6.15 (m, 1 H, C=CH_2), 5.74–5.73 (m, 1 H, C=CH_2), 4.63–4.61 (m, 2 H, OCH_2), 3.76–3.74 (m, 2 H, NCH_2), 3.44–3.40 (m, 2 H, NCH_2), 3.17 (s, 6 H, 2 × NCH_3), 2.82–2.79 (m, 2 H, CH_2SO_3), 1.97 (s, 3 H, H_2C=CCH_3), 1.86–1.78 (m, 4 H, 2 × CH_2), 1.57–1.51 (m, 2 H, CH_2), 1.45–1.39 (m, 2 H, CH_2) ppm. ^{13}C NMR (125 MHz, MeOD): δ = 167.69 (C_{quat}, C=O), 137.15 (C_{quat}, C=CH_2), 127.35 (–, C=CH_2), 66.56 (–, CH_2), 63.88 (–, CH_2), 59.11 (–, CH_2), 52.25 (–, CH_2), 51.90 (+, 2 × NCH_3), 28.86 (–, CH_2), 26.78 (–, CH_2), 25.58 (–, CH_2), 23.18 (–, CH_2), 18.41 (+, H_2C=CCH_3) ppm. FTIR (ATR): $\tilde{\nu}$ = 3411 (w), 3036 (w), 2935 (w), 2862 (w), 1723 (m), 1642 (w), 1466 (w), 1321 (w), 1182 (s), 1159 (s), 1033 (s), 958 (w), 930 (m), 882 (m), 799 (m), 746 (m), 727 (m), 606 (s), 523 (m), 488 (w) cm^{-1}. MS (FAB): *m/z* (%) = 322.2 (100) [M + H]$^+$, 240.3 (16), 113.4 (94) [M – $C_8H_{18}NSO_3$]$^+$. HRMS (FAB): *m/z* calcd. for $C_{14}H_{28}NO_5S$ [M + H]$^+$ 322.1688; found 322.1686. $C_{14}H_{27}NO_5S$ (321.43): calcd. C 52.31, H 8.47, N 4.36, S 9.98; found C 49.69, H 8.30, N 3.82, S 10.01.

8-{[2-(Methacryloyloxy)ethyl]dimethylammonio}octane-1-sulfonate (5f): The reaction was carried out starting from 8-[(2-hydroxyethyl)dimethylammonio]octane-1-sulfonate (**4f**) and following General

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Procedure D, yield 1.55 g (4.44 mmol, 74%); R_f = 0.18 (CH_2Cl_2/MeOH, 1:1). ^{1}H NMR (500 MHz, MeOD): δ = 6.15 (s, 1 H, C=CH_2), 5.73 (s, 1 H, C=CH_2), 4.62 (br. s, 2 H, OCH_2), 3.75–3.74 (m, 2 H, NCH_2), 3.42–3.38 (m, 2 H, NCH_2), 3.17 (s, 6 H, 2 × NCH_3), 2.80–2.77 (m, 2 H, CH_2SO_3), 1.97 (s, 3 H, H_2C=CCH_3), 1.85–1.75 (m, 4 H, 2 × CH_2), 1.50–1.35 (m, 8 H, 4 × CH_2) ppm. ^{13}C NMR (125 MHz, MeOD): δ = 167.69 (C_{quat}, C=O), 137.14 (C_{quat}, C=CH_2), 127.36 (–, C=CH_2), 66.66 (–, CH_2), 63.82 (–, CH_2), 59.10 (–, CH_2), 52.52 (–, CH_2), 51.91 (+, 2 × NCH_3), 29.76 (–, CH_2), 29.65 (–, CH_2), 29.31 (–, CH_2), 27.14 (–, CH_2), 25.79 (–, CH_2), 23.47 (–, CH_2), 18.41 (+, H_2C=CCH_3) ppm. FTIR (ATR): $\tilde{\nu}$ = 2923 (w), 2854 (w), 1717 (m), 1638 (vw), 1466 (w), 1293 (w), 1173 (s), 1035 (m), 967 (w), 938 (w), 915 (w), 843 (vw), 811 (w), 787 (w), 725 (w), 663 (vw), 603 (m), 542 (w), 523 (m) cm^{-1}. MS (FAB): *m/z* (%) = 350.2 (100) $[M + H]^+$, 268.2 (15), 156.1 (8), 114.1 (9), 113.1 (90) $[M - C_{10}H_{22}NSO_3]^+$. HRMS (FAB): *m/z* calcd. for $C_{16}H_{32}NO_5S$ $[M + H]^+$ 350.1996; found 350.1994. $C_{16}H_{31}NO_5S$ (349.48): calcd. C 54.99, H 8.94, N 4.01, S 9.17; found C 51.09, H 9.40, N 3.69, S 8.56.

12-{[2-(Methacryloyloxy)ethyl]dimethylammonio}dodecane-1-sulfonate (5g): The reaction was carried out starting from 12-[(2-hydroxyethyl)dimethylammonio]dodecane-1-sulfonate (**4g**) and following General Procedure D, yield 1.73 g (4.26 mmol, 71%); R_f = 0.28 (CH_2Cl_2/MeOH, 1:1). ^{1}H NMR (500 MHz, MeOD): δ = 6.16–6.15 (m, 1 H, C=CH_2), 5.74–5.72 (m, 1 H, C=CH_2), 4.62–4.60 (m, 2 H, OCH_2), 3.76–3.74 (m, 2 H, NCH_2), 3.43–3.39 (m, 2 H, NCH_2), 3.17 (s, 6 H, 2 × NCH_3), 2.79–2.76 (m, 2 H, CH_2SO_3), 1.97 (s, 3 H, H_2C=CCH_3), 1.83–1.76 (m, 4 H, 2 × CH_2), 1.44–1.33 (m, 16 H, 8 × CH_2) ppm. ^{13}C NMR (125 MHz, MeOD): δ = 167.69 (C_{quat}, C=O), 137.15 (C_{quat}, C=CH_2), 127.34 (–, C=CH_2), 66.66 (–, CH_2), 63.79 (–, CH_2), 59.12 (–, CH_2), 52.74 (–, CH_2), 51.92 (+, 2 × NCH_3), 30.26 (–, 2 × CH_2), 30.11 (–, 2 × CH_2), 30.08 (–, CH_2), 29.61 (–, 2 × CH_2), 27.36 (–, CH_2), 25.90 (–, CH_2), 23.61 (–, CH_2), 18.43 (+, H_2C=CCH_3) ppm. FTIR (ATR): $\tilde{\nu}$ = 2918 (m), 2846 (w), 1715 (m), 1636 (w), 1484 (m), 1466 (m), 1303 (m), 1206 (m), 1178 (s), 1037 (m), 952 (m), 908 (w), 850 (w), 815 (w), 793 (w), 782 (w), 725 (w), 663 (w), 603 (m), 542 (m), 522 (m), 492 (w) cm^{-1}. MS (FAB): *m/z* (%) = 406.1 (100) $[M + H]^+$, 324.2 (8), 154.3 (9), 113.4 (34) $[M - C_{14}H_{30}NSO_3]^+$. HRMS (FAB): *m/z* calcd. for $C_{20}H_{40}NO_5S$ $[M + H]^+$ 406.2627; found 406.2629. $C_{20}H_{39}NO_5S$ (405.59): calcd. C 59.23, H 9.69, N 3.45, S 7.91; found C 57.53, H 9.72, N 3.14, S 7.78.

Supporting Information (see footnote on the first page of this article): Experimental details, analytical equipment, GPC data analysis of the zwitterionic polymers, as well as ^{1}H and ^{13}C NMR spectra of all compounds.

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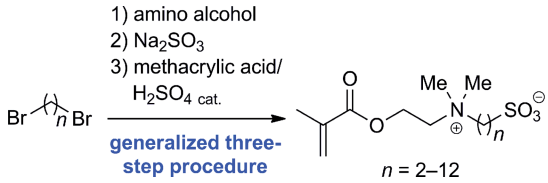

A simple and highly universal three-step procedure has been developed for the synthesis of sulfobetaine methacrylates with variation of the charge separation distance. The protocol provides access to a library of new zwitterionic precursors that have potential for a range of applications in polymer chemistry and materials science.

Keywords: Synthetic methods / Materials science / Surfactants / Zwitterions / Polymerization

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