Synthesis of Quaternary Alkylammonium Sulfobetaines

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Abstract: A series of quaternary alkylammonium sulfobetaines of general formula $RN^+(CH_3)_2(CH_2)_nSO_3^-$, where n = 2–4, have been synthesised by reacting the corresponding *N*,*N*-dimethylamines with either sodium 2-chloroethanesulfonate (n = 2), 1,3-propanesultone (n = 3), or 1,4-butanesultone (n = 4). Full details of the preparation of the required *N*,*N*-dimethylamines are reported.

Key words: Mannich bases, Friedel–Crafts reactions, zwitterions, sultones, surfactants

In connection with our studies on the determination of log P based QSARs for the aquatic toxicity of zwitterionic and cationic surfactants,[1] we have synthesised a series of zwitterionic compounds **1**–**21** of the ammonium sulfobetaine type (Figure 1). The compounds synthesised belong to three series varying in the length of the spacer unit separating the quaternary ammonium centre from the sulfonate group. In addition, compounds **7**– **12** and **16**–**21** all contain an aromatic ring which is separated from the quaternary ammonium centre by up to four CH_2 groups and, in the case of **11**, **12**, **20**, and **21**, the aromatic ring carries a *para* alkyl substituent.

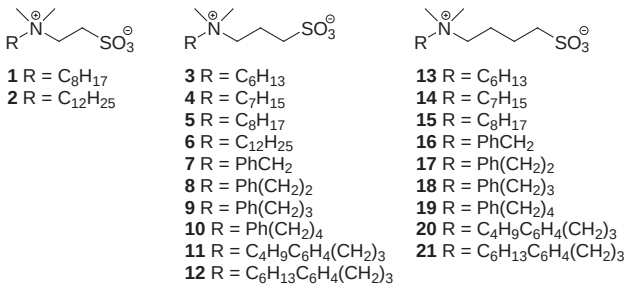
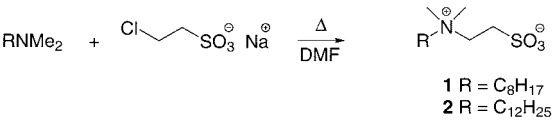


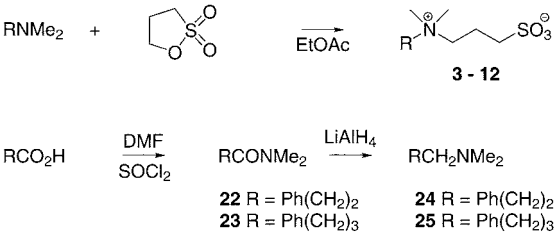
Figure 1

The two ethane sulfobetaines, **1** and **2**, were synthesised by reacting commercially available *N*,*N*-dimethylamines with sodium 2-chloroethanesulfonate at reflux in DMF for 96 hours (Scheme 1). The products separated on cooling as finely powdered white solids and were isolated by filtration.



Scheme 1

The propane sulfobetaines (**3**– **12**) were prepared by reacting the corresponding *N*,*N*-dimethylamines with 1,3-propanesultone in ethyl acetate at room temperature (Scheme 2).[2,3] The products separated out from the solution as white solids which could be purified by recrystallisation. The amines required for the preparation of **3**–**8** were commercially available, while *N*,*N*-dimethyl-3-phenylpropylamine (**24**) and *N*,*N*-dimethyl-4-phenylbutylamine (**25**) were prepared by reducing the corresponding *N*,*N*-dimethylamides **22** and **23** with $LiAlH_4$ (Scheme 2).[4] The dimethylamides **22** and **23** in turn were prepared from hydrocinnamic acid and 3-phenylbutanoic acid respectively by reaction with DMF and thionyl chloride. The direct preparation of an *N*,*N*-dimethylamide by reacting a carboxylic acid with DMF and a co-reagent such as P_2O_5,[5–8] $POCl_3$,[9,10] $(COCl)_2$,[11–14] DCCI[15,16] or NaH[17] has been previously reported but, to the best of our knowledge, there are only two reports of the use of $SOCl_2$ for this purpose.[18,19]



Scheme 2

For the synthesis of the amines required for the preparation of **11** and **12** we initially intended to make use of a Mannich reaction[20] to make the ketones **27** and **28** (Scheme 3), but all attempts to carry out a Mannich reaction on 4-hexylacetophenone (**26**) proved unsuccessful. Furthermore, attempts to carry out Friedel–Crafts acylation on *N*,*N*-dimethyl-3-phenylpropylamine (**24**) using hexanoyl chloride also proved unsuccessful. We therefore decided to investigate the possibility of synthesising the ketones **27** and **28** by means of a conjugate addition

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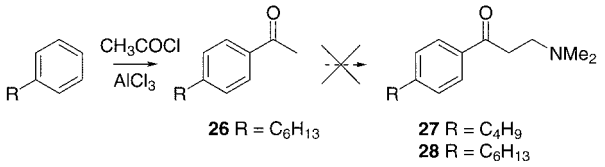
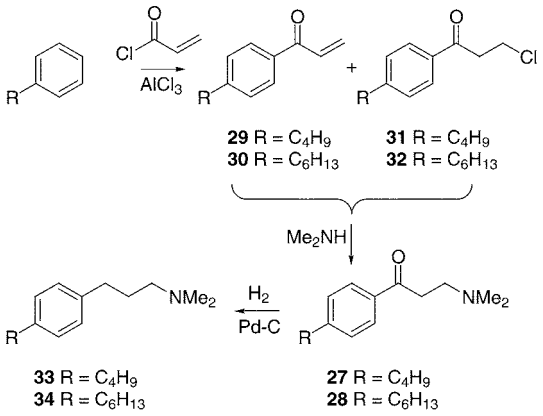
reaction[21] on the α,β-unsaturated ketones **29** and **30** (Scheme 4). The unsaturated ketone **29** was obtained along with the 3-chloropropiophenone derivative **31** by reacting butylbenzene with acryloyl chloride.[22] Similarly, reaction of 1-phenylhexane with acryloyl chloride afforded a mixture of the unsaturated ketone **30** and the chloro ketone **32**. In each case, the relative proportions of the two products varied with the reaction conditions, but they reacted, without separation, with dimethylamine to give the corresponding dimethylamino ketones **27** and **28**. Hydrogenation of **27** and **28** gave the required dimethyl amines **33** and **34** which reacted with 1,3-propanesultone to afford the zwitterionic compounds **11** and **12** (Scheme 2).

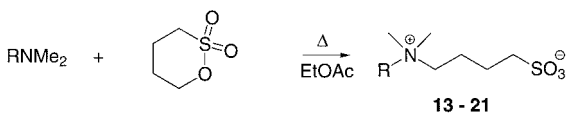


Scheme 3



Scheme 4

The butane sulfobetaines **13–21** were prepared by reacting the corresponding *N,N*-dimethylamines with 1,4-butanesultone in ethyl acetate under reflux (Scheme 5).[2,3] The products separated out from the solution as white solids which were purified by washing with ether.



Scheme 5

In conclusion, a series of quaternary alkylammonium sulfobetaines have been synthesised by reacting the corresponding tertiary amines with either sodium 2-chloroethanesulfonate or with an appropriate sultone. The products were obtained as white hygroscopic solids which were stored under anhydrous conditions until required. We are currently measuring log P values of these compounds using a variety of direct and indirect analytical methods and obtaining aquatic toxicity data. The results of these determinations and the correlation of log P with aquatic toxicity will be reported separately in due course.

^{1}H and ^{13}C NMR spectra were recorded on a Bruker AC 400 instrument and were run in $CDCl_3$ unless otherwise stated. Mass spectra were recorded on a VG 12−250 low resolution quadrupole instrument or on a VG Micromass Quattro II instrument. Accurate mass measurements were made using either a ZAB-E high resolution double-focussing instrument or a Finnigan Mat 900 instrument. Melting points were recorded on an Electrothermal 9100 apparatus and are uncorrected.

TLC analysis was carried out on Merck 5785 Kiesegel $60F_{254}$ fluorescent plates. Flash chromatography was performed on silica gel (Fisons Matrex, 35–70 μ). Et_2O and CH_2Cl_2 were dried by passing them down an alumina column and distillation from calcium hydride. THF was passed down an alumina column and distilled from sodium/benzophenone.

Ethane Sulfobetaines 1 and 2; General Procedure

***N*-Octyl-*N,N*-dimethyl-2-ammonio-1-ethanesulfonate (1)**

To a stirred soln of sodium 2-chloroethanesulfonate monohydrate (8.809 g, 47.6 mmol) in DMF (75 mL), was added a soln of *N,N*-dimethyloctylamine (7.404 g, 47.2 mmol) in DMF (75 mL). The reaction mixture was stirred under reflux for 96 h before cooling to r.t. The resulting precipitate was filtered, washed with Et_2O, and dried in vacuo to yield the product **1** as a finely powdered white solid (3.313 g, 27%); mp 242–244 °C.

^{1}H NMR (400 MHz, CD_3OD): δ = 0.86 (t, 3 H, *J* = 6.8 Hz, CH_3), 1.20–1.32 [m, 10 H, $(CH_2)_5$], 1.62 (m, 2 H, C*H*$_2$CH$_2$N), 2.92 (m, 2 H, CH_2SO_3) 3.02 [s, 6 H, $N(CH_3)_2$], 3.26 (m, 2 H, CH_2N), 3.51 (m, 2 H, NCH_2).

^{13}C NMR (101 MHz, CD_3OD): δ = 14.0 (CH_3), 21.7 (CH_2), 22.1 (CH_2), 25.8 (CH_2), 28.5 (CH_2), 28.5 (CH_2), 31.2 (*C*H$_2$CH$_2$N), 44.3 (CH_2SO_3), 50.1 (NCH_3), 60.0 (NCH_2), 62.7 (CH_2N).

MS-EI: *m*/*z* = 264 (1%) $[M - H]^+$, 158 (16%), 157 (100%), 156 (10%).

MS-CI: *m*/*z* = 266 (1%) $[M + H]^+$, 159 (9%), 158 (100%).

HRMS: *m*/*z* calcd for $C_{12}H_{28}NSO_3$ $[M + H]^+$, 266.1790; found, 266.1786.

***N*-Dodecyl-*N,N*-dimethyl-2-ammonio-1-ethanesulfonate (2)**

Prepared using the procedure described above starting from *N,N*-dimethyldodecylamine (10.77 g, 50.6 mmol). The product **2** was obtained as a finely powdered white solid (2.575 g, 16%); mp 357–358 °C (lit.[23] mp 353 °C).

^{1}H NMR (400 MHz, CD_3OD): δ = 0.90 (t, 3 H, *J* = 6.9 Hz, CH_3), 1.24–1.40 [m, 18 H, $(CH_2)_9$], 1.80 (m, 2 H, C*H*$_2$CH$_2$N), 3.09 [s, 6 H, $N(CH_3)_2$], 3.30 (m, 4 H, CH_2SO_3 and CH_2N), 3.70 (m, 2 H, NCH_2).

^{13}C NMR (101 MHz, CD_3OD): δ = 15.0 (CH_3), 24.0, 24.1, 27.7, 30.6, 30.8, 30.9, 31.0, 31.1 (8 × CH_2), 33.4 (*C*H$_2$CH$_2$N), 46.0 (CH_2SO_3), 52.4 (NCH_3), 61.3 (NCH_2), 66.4 (CH_2N).

MS-FAB: *m*/*z* = 665 (7%) $[2 M + Na]^+$, 643 (3%) $[2 M + H]^+$, 344 (74%) $[M + Na]^+$, 322 (86%) $[M + H]^+$, 228 (52%), 214 (100%).

HRMS (ES^+): *m*/*z* calcd for $C_{16}H_{36}NSO_3$ $[M + H]^+$, 322.2416; found, 322.2411.

Propane Sulfobetaines 3–8; General Procedure

***N*-Hexyl-*N,N*-dimethyl-3-ammonio-1-propanesulfonate (3)**

To a stirred soln of 1,3-propanesultone (9.879 g, 81.0 mmol) in EtOAc (30 mL), was added *N,N*-dimethylhexylamine (10.476 g,

81.2 mmol) in EtOAc (30 mL). The reaction mixture was stirred at r.t. for 1.5 h. The resulting white precipitate was filtered, washed with Et_2O, and dried in vacuo to yield **3** (12.79 g, 63%) as a white crystalline solid.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.88 (t, 3 H, *J* = 6.9 Hz, CH_3), 1.28–1.37 [m, 6 H, $(CH_2)_3$], 1.72 (m, 2 H, C*H*$_2$CH$_2$N), 2.21 (m, 2 H, C*H*$_2$CH$_2$SO$_3$), 2.87 (t, 2 H, *J* = 6.9 Hz, CH_2SO_3), 3.19 [s, 6 H, $N(CH_3)_2$], 3.30 (m, 2 H, CH_2N), 3.68 (m, 2 H, NCH_2).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 13.9 (CH_3), 19.4, 22.4, 22.6 (3 × CH_2), 26.0 (NCH_2CH_2), 31.2 (*C*H$_2$CH$_2$N), 47.8 (CH_2SO_3), 50.8 (NCH_3), 63.1 (NCH_2), 64.3 (CH_2N).

MS-EI: *m*/*z* = 251 (1%) [M$^+$], 250 (2%) [M – H]$^+$, 180 (4%), 166 (2%), 130 (19%), 129 (100%).

MS-CI: *m*/*z* = 252 (1%) [M + H]$^+$, 238 (3%), 182 (1%), 140 (30%), 130 (100%).

HRMS: *m*/*z* calcd for $C_{11}H_{26}NSO_3$ [M + H]$^+$, 252.1633; found, 252.1630.

***N*-Heptyl-*N*,*N*-dimethyl-3-ammonio-1-propanesulfonate (4)**
Prepared using the procedure described above starting from *N*,*N*-dimethylheptylamine (9.804 g, 68.6 mmol). The product **4** was obtained as a white crystalline solid (12.30 g, 68%); mp 188–191 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.88 (t, 3 H, *J* = 6.9 Hz, CH_3), 1.27–1.34 [m, 8 H, $(CH_2)_4$], 1.72 (m, 2 H, C*H*$_2$CH$_2$N), 2.22 (m, 2 H, C*H*$_2$CH$_2$SO$_3$), 2.88 (t, 2 H, *J* = 6.8 Hz, CH_2SO_3), 3.18 [s, 6 H, $N(CH_3)_2$], 3.28 (m, 2 H, CH_2N), 3.66 (m, 2 H, NCH_2).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 14.1 (CH_3), 19.1 (CH_2), 22.5 (CH_2), 22.6 (CH_2), 26.3 (NCH_2CH_2), 28.9 (CH_2), 31.6 (*C*H$_2$CH$_2$N), 47.8 (CH_2SO_3), 50.8 (NCH_3), 63.0 (NCH_2), 64.3 (CH_2N).

MS-EI: *m*/*z* = 265 (1%) [M$^+$], 264 (3%) [M – H]$^+$, 180 (18%), 166 (6%), 144 (18%), 143 (100%).

MS-CI: *m*/*z* = 266 (2%) [M + H]$^+$, 252 (2%), 184 (2%), 182 (2%), 170 (6%), 145 (8%), 144 (100%), 140 (30%).

HRMS: *m*/*z* calcd for $C_{12}H_{28}NSO_3$ [M + H]$^+$, 266.1790; found, 266.1788.

***N*-Octyl-*N*,*N*-dimethyl-3-ammonio-1-propanesulfonate (5)**
Prepared using the procedure described above starting from *N*,*N*-dimethyloctylamine (10.61 g, 67.6 mmol). The product **5** was obtained as a white crystalline solid (12.69 g, 67%); mp 203–204 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.86 (t, 3 H, *J* = 6.7 Hz, CH_3), 1.24–1.32 [m, 10 H, $(CH_2)_5$], 1.70 (m, 2 H, C*H*$_2$CH$_2$N), 2.20 (m, 2 H, C*H*$_2$CH$_2$SO$_3$), 2.86 (t, 2 H, *J* = 6.5 Hz, CH_2SO_3), 3.19 [s, 6 H, $N(CH_3)_2$], 3.28 (m, 2 H, CH_2N), 3.68 (m, 2 H, NCH_2).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 14.1 (CH_3), 19.4 (CH_2), 22.6 (CH_2), 22.7 (CH_2), 26.3 (NCH_2CH_2), 29.1 (CH_2), 29.2 (CH_2), 31.7 (*C*H$_2$CH$_2$N), 47.8 (CH_2SO_3), 50.8 (NCH_3), 63.2 (NCH_2), 64.3 (CH_2N).

MS-EI: *m*/*z* = 278 (6%) [M – H]$^+$, 180 (72%), 166 (75%), 157 (100%), 156 (94%).

MS-CI: *m*/*z* = 280 (4%) [M + H]$^+$, 266 (3%), 184 (4%), 170 (3%), 159 (25%), 158 (100%), 140 58%).

HRMS: *m*/*z* calcd for $C_{13}H_{30}NSO_3$ [M + H]$^+$, 280.1946; found, 280.1945.

***N*-Dodecyl-*N*,*N*-dimethyl-3-ammonio-1-propanesulfonate (6)**
To a stirred soln of 1,3-propanesultone (2.526 g, 20.7 mmol) in EtOAc (50 mL), was added *N*,*N*-dimethyldodecylamine (3.815 g, 17.9 mmol) in EtOAc (50 mL). The reaction mixture was stirred at r.t. for 24 h. The resulting white precipitate was filtered, washed with Et_2O, and dried in vacuo to yield **6** (2.407 g, 68%) as a white crystalline solid; mp 242–4 °C (lit.[24] mp 250–255 °C).

^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.78 (t, 2 H, *J* = 6.8 Hz, CH_3), 1.08–1.27 [m, 18 H, $(CH_2)_9$], 1.60 (m, 2 H, C*H*$_2$CH$_2$N), 2.10 (m, 2 H, C*H*$_2$CH$_2$SO$_3$), 2.88 (t, 2 H, *J* = 6.7 Hz, CH_2SO_3), 3.10 [s, 6 H, $N(CH_3)_3$], 3.15 (m, 2 H, CH_2N), 3.60 (m, 2 H, NCH_2).

^{13}C NMR (63 MHz, $CDCl_3$): δ = 14.0 (CH_3), 19.3, 22.6, 26.3 (3 × CH_2), 26.3 (NCH_2CH_2), 29.1, 29.2, 29.4, 29.4, 29.5, (5 × CH_2), 31.8 (*C*H$_2$CH$_2$N), 47.7 (CH_2SO_3), 50.7 (NCH_3), 63.2 (NCH_2), 64.3 (CH_2N).

MS-EI: *m*/*z* = 335 (27%) [M$^+$], 213 (100%), 212 (48%).

MS-CI: *m*/*z* = 336 (1%) [M + H]$^+$, 214 (100%).

***N*-Benzyl-*N*,*N*-dimethyl-3-ammonio-1-propanesulfonate (7)**
To a stirred soln of 1,3-propanesultone (1.113 g, 9.12 mmol) in EtOAc (15 mL), was added *N*,*N*-dimethylbenzylamine (1.117 g, 8.27 mmol) in EtOAc (15 mL). The reaction mixture was stirred at r.t. for 12 h. The resulting white precipitate was filtered, washed with Et_2O, and dried in vacuo to yield **7** (1.416 g, 67%) as a white crystalline solid; mp 235–237 °C.

^{1}H NMR (400 MHz, CD_3OD): δ = 2.33 (m, 2 H, C*H*$_2$CH$_2$SO$_3$), 2.90 (t, 2 H, *J* = 6.9 Hz, CH_2SO_3), 3.04 [s, 6 H, $N(CH_3)_2$], 3.54 (m, 2 H, NCH_2), 4.55 (s, 2 H, $PhCH_2N$), 7.50–7.60 (m, 5 H, C_6H_5).

^{13}C NMR (101 MHz, CD_3OD): δ = 20.0 (NCH_2CH_2), 48.7 (CH_2SO_3), 50.2 (NCH_3), 64.3 (NCH_2), 68.9 (CH_2N), 128.8 (Ph, C-1), 130.3, 131.8, 134.1 (Ph, 3 × CH).

MS-EI: *m*/*z* = 257 (1%) [M$^+$], 256 (1%) [M – H]$^+$, 182 (100%), 135 (25%), 105 (65%).

MS-CI: *m*/*z* = 258 (3%) [M + H]$^+$, 185 (13%), 168 (30%), 140 (20%), 136 (100%).

(MS-ES$^+$): *m*/*z* = 537 (13%), [2 M + Na]$^+$, 515 (5%) [2 M + H]$^+$, 280 (100%) [M + Na]$^+$, 258 (55%) [M + H]$^+$.

(MS-ES$^-$): *m*/*z* = 302 (78%), 292 (52%) [M + Cl]$^-$, 256 (19%) [M–H]$^-$.

HRMS (ES$^+$): *m*/*z* calcd for $C_{12}H_{20}NSO_3$ [M + H]$^+$, 258.1164; found, 258.1163.

***N*-Phenylethyl-*N*,*N*-dimethyl-3-ammonio-1-propanesulfonate (8)**
To a stirred soln of 1,3-propanesultone (4.207 g, 34.5 mmol) in EtOAc (70 mL), was added *N*,*N*-dimethylphenethylamine (5.138 g, 34.5 mmol) in EtOAc (70 mL). The reaction mixture was stirred at r.t. for 112 h. The resulting white precipitate was filtered, washed with Et_2O, and dried in vacuo to yield **8** (6.353 g, 68%) as a white crystalline solid; mp 244–246 °C.

^{1}H NMR (400 MHz, CD_3OD): δ = 2.24 (m, 2 H, C*H*$_2$CH$_2$SO$_3$), 2.89 (t, 2 H, *J* = 6.8 Hz, CH_2SO_3), 3.10–3.16 (m, 2 H, $PhCH_2$), 3.17 [s, 6 H, $N(CH_3)_2$], 3.53 (m, 2 H, NCH_2), 3.61 (m, 2 H, CH_2N), 7.24–7.36 (m, 5 H, C_6H_5).

^{13}C NMR (101 MHz, CD_3OD): δ = 19.9 (NCH_2CH_2), 29.7 ($ArCH_2$), 48.5 (CH_2SO_3), 51.4 (NCH_3), 63.6 (NCH_2), 65.9 (CH_2N),128.3, 129.9, 130.1 (Ph, 3 × CH), 137.0 (Ph, C-1).

MS-EI: *m*/*z* = 271 (20%) [M$^+$], 270 (100%) [M – H]$^+$, 231 (53%).

MS-CI: *m*/*z* = 272 (70%) [M + H]$^+$, 258 (100%).

HRMS (ES$^+$): *m*/*z* calcd for $C_{13}H_{30}NSO_3$ [M + H]$^+$, 272.1320; found, 272.1318.

***N*-Phenylpropyl-*N*,*N*-dimethyl-3-ammonio-1-propanesulfonate (9)**

N,*N*-Dimethyl-3-phenylpropanamide (**22**)
To a stirred soln of 3-phenylpropionic acid (2.000 g, 13.3 mmol) in DMF (15 mL, 0.19 mol) at 0 °C, was added SO_2Cl_2 (2 mL, 27.0 mmol). The reaction mixture was stirred for 1.75 h as the tempera-

ture was raised from 40 to 90 °C. HCl evolved was trapped by bubbling into 1 M aq Na_2CO_3. Excess $SOCl_2$ and DMF were removed by reduced pressure distillation (20 °C, 1.5 mm Hg) and the crude product was dissolved in CH_2Cl_2 (50 mL). The organic layer was washed with H_2O (3 × 50 mL) and the CH_2Cl_2 removed in vacuo to yield **22** (2.199 g, 93%) as a brown oil.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.50–2.56 (m, 2 H, $PhCH_2CH_2$), 2.84 (s, 3 H, NCH_3), 2.87 (s, 3 H, NCH_3), 2.88–2.95 (m, 2 H, $PhCH_2$), 7.14–7.25 (m, 5 H, C_6H_5).

^{13}C NMR (63 MHz, $CDCl_3$): δ = 31.3 (CH_2CO), 35.2 ($ArCH_2$), 35.3 (NCH_3), 37.1 (NCH_3), 126.0, 128.3, 128.4 (Ph, 3 × CH), 141.4 (Ph, C-1), 172.1 (CO).

MS-EI: *m*/*z* = 177 (56%) [M^+], 105 (67%), 104 (62%), 91 (100%).

MS-CI: *m*/*z* = 195 (28%) [M + NH_4]$^+$, 178 (100%) [M + H]$^+$.

HRMS (ES^+): *m*/*z* calcd for $C_{11}H_{16}NO$ [M + H]$^+$, 178.1232; found, 178.1232.

N,*N*-Dimethyl-3-phenylpropylamine (**24**)
To a stirred suspension of $LiAlH_4$ (1.550 g, 40.8 mmol) in anhyd THF (20 mL), under N_2, was added dropwise a soln of **22** (2.094 g, 11.8 mmol) in anhyd THF (10 mL). The reaction mixture was stirred under gentle reflux for 5 h. After cooling, the excess $LiAlH_4$ and metallic complexes were deposited by the careful addition of acetone (3 mL) to the well-stirred mixture. An equal volume of anhyd Et_2O was added, followed by the careful dropwise addition of H_2O (2 mL) after which the mixture was filtered and the solid residue washed with Et_2O (20 mL). The filtrate was dried over anhyd $MgSO_4$ and the THF–Et_2O solvent mixture removed in vacuo to yield 24 (1.923 g, 74%) as a dark yellow liquid.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.71 (q^5, 2 H, *J* = 7.7 Hz, $PhCH_2CH_2$), 2.13 [s, 6 H, $N(CH_3)_2$], 2.20(t, 2 H, *J* = 7.7 Hz, CH_2N), 2.54 (t, 2 H, *J* = 7.7 Hz, $PhCH_2$), 7.08–7.18 (m, 5 H, C_6H_5).

^{13}C NMR (63 MHz, $CDCl_3$): δ = 29.4 (CH_2CH_2N), 35.6 ($ArCH_2$), 45.4 (NCH_3), 59.2 (CH_2N), 125.6, 128.2, 128.3 (Ph, 3 × CH), 142.2 (Ph, C-1).

MS-EI: *m*/*z* = 163 (100%) [M^+].

MS-CI: *m*/*z* = 164 (100%) [M + H]$^+$.

HRMS (ES^+): *m*/*z* calcd for $C_{11}H_{18}N$ [M + H]$^+$, 164.1439; found, 164.1439.

N-Phenylpropyl-*N*,*N*-dimethyl-3-ammonio-1-propanesulfonate (**9**)
To a stirred soln of 1,3-propanesultone (0.500 g, 4.1 mmol) in EtOAc (10 mL), was added a soln of **24** (0.534 g, 3.3 mmol) in EtOAc (10 mL). The reaction mixture was stirred at r.t. for 140 h. The resulting white precipitate was filtered, washed with Et_2O, and dried in vacuo to yield **9** (0.531 g, 57%) as a white crystalline solid; mp 172–7 °C.

^{1}H NMR (400 MHz, CD_3OD): δ = 2.10–2.21 (m, 4 H, $PhCH_2CH_2$ and $CH_2CH_2SO_3$), 2.73 (t, 2 H, *J* = 7.55 Hz, $PhCH_2$), 2.87 (t, 2 H, *J* = 7.0 Hz, CH_2SO_3), 3.10 [s, 6 H, $N(CH_3)_2$], 3.35 (m, 2 H, NCH_2), 3.52 (m, 2 H, CH_2N), 7.20–7.35 (m, 5 H, C_6H_5).

^{13}C NMR (101 MHz, CD_3OD): δ = 19.9 (NCH_2CH_2), 25.2 (CH_2CH_2N), 33.2 ($ArCH_2$), 48.6 (CH_2SO_3), 51.4 (NCH_3), 63.8 (NCH_2), 65.0 (CH_2N), 127.6, 129.5, 129.7 (Ph, 3 × CH), 141.3 (Ph, C-1).

MS-EI: *m*/*z* = 286 (44%) [M + H]$^+$, 285 (57%) [M^+], 284 (100%) [M – H]$^+$, 190 (47%).

MS-CI: *m*/*z* = 286 (58%) [M + H]$^+$, 272 (100%), 192 (87%), 190 (92%), 178 (42%).

HRMS (ES^+): *m*/*z* calcd for $C_{14}H_{24}NSO_3$ [M + H]$^+$, 286.1477; found, 286.1475.

N-Phenylbutyl-*N*,*N*-dimethyl-3-ammonio-1-propanesulfonate (10)
N,*N*-Dimethyl-4-phenylbutanamide (23)
To a stirred soln of 4-phenylbutyric acid (3.285 g, 20.0 mmol) in DMF (15 mL, 0.19 mol) at 0 °C, was added SO_2Cl_2 (2 mL, 27.0 mmol). The reaction mixture was stirred for 1.75 h as the temperature was raised from 40–90 °C. HCl evolved was trapped by bubbling into 1 M aq Na_2CO_3. Excess $SOCl_2$ and DMF were removed by reduced pressure distillation (20 °C, 1.5 mm Hg) and the crude product was dissolved in CH_2Cl_2 (50 mL). The organic layer was washed with H_2O (3 × 50 mL) and the CH_2Cl_2 removed in vacuo to yield **23** (3.629 g, 95%) as a brown oil.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.87 (q^5, 2 H, *J* = 7.5 Hz, $PhCH_2CH_2$), 2.21 (t, 2 H, *J* = 7.5 Hz, $PhCH_2$), 2.57 (t, 2 H, *J* = 7.5 Hz, CH_2CO), 2.83 [s, 6 H, $N(CH_3)_2$], 7.06–7.20 (m, 5 H, C_6H_5).

^{13}C NMR (63 MHz, $CDCl_3$): δ = 26.5 ($ArCH_2CH_2$), 32.4 (CH_2CO), 35.2 ($ArCH_2$), 35.3 (NCH_3), 37.2 (NCH_3), 125.8, 128.2, 128.4 (Ph, 3 × CH), 141.7 (Ph, C-1), 170.3 (CO).

MS-EI: *m*/*z* = 191 (100%) [M^+], 147 (17%).

MS-CI: *m*/*z* = 209 (12%) [M + NH_4]$^+$, 192 (100%) [M + H]$^+$.

HRMS (ES^+): *m*/*z* calcd for $C_{12}H_{18}NO$ [M + H]$^+$, 192.1388; found, 192.1386.

N,*N*-Dimethyl-4-phenylbutylamine (**25**)
To a stirred suspension of $LiAlH_4$ (0.959 g, 25.2 mmol) in anhyd THF (20 mL), under N_2, was added dropwise a soln of **23** (2.60 g, 13.6 mmol) in anhyd THF (10 mL). The reaction mixture was stirred under gentle reflux for 5 h. After cooling, the excess $LiAlH_4$ and metallic complexes were deposited by the careful addition of acetone (3 mL) to the well-stirred mixture. An equal volume of anhyd Et_2O was added, followed by the careful dropwise addition of H_2O (2 mL) after which the mixture was filtered and the solid residue washed with Et_2O (20 mL). The filtrate was dried over anhyd $MgSO_4$ and the THF–Et_2O solvent mixture removed in vacuo to yield **25** (2.201 g, 91%) as a dark yellow liquid.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.39 (q^5, 2 H, *J* = 7.6 Hz, $PhCH_2CH_2$),1.56 (q^5, 2 H, *J* = 7.6 Hz, CH_2CH_2N), 2.09 [s, 6 H, $N(CH_3)_2$], 2.18 (t, 2 H, *J* = 7.5 Hz, $PhCH_2$), 2.52 (t, 2 H, *J* = 7.5, CH_2N), 7.06–7.20 (m, 5 H, C_6H_5).

^{13}C NMR (63 MHz, $CDCl_3$): δ = 27.3 (CH_2), 35.8 (CH_2), 39.2 (CH_2), 45.4 (NCH_3), 59.6 (CH_2N), 125.6 (Ph, CH), 128.2 (Ph, CH), 128.3 (Ph, CH), 142.4 (Ph, C-1).

MS-EI: *m*/*z* = 177 (100%) [M^+].

MS-CI: *m*/*z* = 178 (100%) [M + H]$^+$.

HRMS (ES^+): *m*/*z* calcd for $C_{12}H_{20}N$ [M + H]$^+$, 178.1595; found, 178.1596.

N-Phenylbutyl-*N*,*N*-dimethyl-3-ammonio-1-propanesulfonate (**10**)
To a stirred soln of 1,3-propanesultone (1.080 g, 8.9 mmol) in EtOAc (20 mL), was added a soln of **25** (1.126 g, 6.9 mmol) in EtOAc (20 mL). The reaction mixture was stirred at r.t. for 261 h. The resulting white precipitate was filtered, washed with Et_2O, and dried in vacuo to yield **10** (1.027 g, 50%) as a white crystalline solid; mp 188–191 °C.

^{1}H NMR (250 MHz, CD_3OD): δ = 1.62–1.88 [m, 4 H, $PhCH_2(CH_2)_2$], 2.11–2.20 (m, 2 H, $CH_2CH_2SO_3$), 2.71 (t, 2 H, *J* = 7.4 Hz, $PhCH_2$), 2.85 (t, 2 H, *J* = 6.8 Hz, CH_2SO_3), 3.06 [s, 6 H, $N(CH_3)_2$], 3.33 (m, 2 H, NCH_2), 3.45 (m, 2 H, CH_2N), 7.16–7.28 (m, 5 H, C_6H_5).

^{13}C NMR (63 MHz, CD_3OD): δ = 19.9 (NCH_2CH_2), 23.0 ($ArCH_2CH_2$), 29.2 (CH_2CH_2N), 36.1 ($ArCH_2$), 48.6 (CH_2SO_3), 51.2 (NCH_3), 63.8 (NCH_2), 65.2 (CH_2N), 127.1 (Ph, CH), 129.4 (Ph, CH), 129.5 (Ph, CH), 142.8 (Ph, C-1).

MS-EI: *m*/*z* = 299 (27%) [M^+], 298 (69%) [M – H]$^+$, 202 (77%), 192 (100%).

MS-CI: *m*/*z* = 300 (100%) [M + H]$^+$, 286 (97%).

HRMS (ES^+): *m*/*z* calcd for $C_{15}H_{26}NSO_3$ [M + H]$^+$, 300.1633; found, 300.1629.

4-Hexylacetophenone (26)[25]

Acetyl chloride (25.92 g, 0.33 mol) in anhyd CH_2Cl_2 (50 mL) was added dropwise to a suspension of $AlCl_3$ (23.92 g, 0.18 mol) in the same solvent (100 mL) at r.t. To the stirred mixture was added 1-phenylhexane (11.75 g, 72.5 mmol) in anhyd CH_2Cl_2 (50 mL) at r.t. After 22 h, the mixture was poured onto a mixture of ice and concd HCl. The aq soln was separated, extracted with CH_2Cl_2 (3 × 100 mL), the combined organic layers were washed with aq Na_2CO_3 (2 × 120 mL), H_2O (3 × 100 mL) and dried over anhyd $MgSO_4$. The solvent was evaporated under reduced pressure to yield **26** (9.614 g, 65%) as a dark orange liquid.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.78 [t, 3 H, *J* = 6.8 Hz, C*H*$_3$(CH$_2$)$_5$], 1.21 [m, 6 H, CH$_3$(C*H*$_2$)$_3$], 1.53 [q^5, 2 H, *J* = 7.5 Hz, CH$_3$(CH$_2$)$_3$C*H*$_2$], 2.49 (s, 3 H, COCH$_3$), 2.56 (t, 2 H, *J* = 7.7 Hz, ArCH$_2$), 7.17 and 7.78 (2 × d, 4 H, *J* = 8.2 Hz, C_6H_4).

^{13}C NMR (63 MHz, $CDCl_3$): δ = 8.86 (CH_3), 17.36 (CH_2), 21.33 (CO*C*H$_3$), 23.71 (CH_2), 25.88 (CH_2), 26.45 (CH_2), 30.78 (CH_2), 123.25 (Ar, CH), 123.39 (Ar, CH), 129.63 (Ar, C-1/4), 143.57 (Ar, C-1/4), 192.63 (CO).

MS-EI: *m*/*z* = 204 (14%) [M^+], 190 (15%), 189 (100%) [M – CH_3]$^+$.

MS-CI: *m*/*z* = 222 (100%) [M + NH_4]$^+$, 206 (11%), 205 (54%) [M + H]$^+$, 189 (12%).

HRMS: *m*/*z* calcd for $C_{14}H_{20}O$ [M + H]$^+$, 205.1592; found, 205.1594.

***N*-[3-(4-Butylphenyl)propyl]-*N*,*N*-dimethyl-3-ammonio-1-propanesulfonate (11)**

1-(4-Butylphenyl)propenone (**29**) and 3-Chloro-1-(4-butylphenyl)propan-1-one (**31**)

To a suspension of $AlCl_3$ (9.922 g, 74.6 mmol) in anhyd 1,2-dichloroethane (30 mL) at 0 °C under N_2 was added acryloyl chloride (3.7 mL, 4.122 g, 45.3 mmol) in 1, 2-dichloroethane (20 mL). A soln of 1-phenylbutane (5.8 mL, 4.988 g, 37.2 mmol) in 1,2-dichloroethane (20 mL) was added dropwise to the stirred mixture. After stirring in the dark for 5.5 h at r.t., the reaction mixture was poured into a mixture of ice H_2O (50 mL), HCl (12 N, 50 mL) and extracted with CH_2Cl_2 (3 × 100 mL). The combined organic extracts were washed with sat. aq $NaHCO_3$ (3 × 100 mL), brine (2 × 100 mL) and dried over anhyd $MgSO_4$. The filtered soln was evaporated in vacuo to yield **29** (3.115 g, 16.6 mmol) and **31** (4.357 g, 19.5 mmol) in 97% yield (46:54 respectively) as a yellow powdered solid.

29

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.94 (t, 3 H, *J* = 7.3 Hz, CH_3), 1.37 (s^6, 2 H, *J* = 7.4 Hz, CH$_3$C*H*$_2$), 1.59–1.66 (m, 2 H, CH$_3$CH$_2$C*H*$_2$), 2.68 [t, 2 H, *J* = 6.3 Hz, CH$_3$(CH$_2$)$_2$C*H*$_2$], 5.90 (dd, 1 H, *J* = 1.5, 10.6 Hz, CH=CH*H*), 6.44 (dd, 1 H, *J* = 1.7, 15.4 Hz, CH=CH*H*), 7.18 (dd, 1 H, *J* = 10.6, 17.1 Hz, C*H*=CH$_2$), 7.29 and 7.89 (2 × d, 4 H, *J* = 8.3 Hz, C_6H_4).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 14.3 (CH_3), 22.7 (CH$_3$C*H*$_2$), 33.5 (CH$_3$CH$_2$C*H*$_2$), 36.1 (CH$_2$Ar), 128.7 (Ar, CH), 129.2 (Ar, CH), 130.1 (CH_2), 132.8 (CH), 135.3 (Ar, C-1/4), 149.8 (Ar, C-1/4), 190.9 (CO).

MS-EI: *m*/*z* = 188 (5%) [M^+], 161 (100%), 91 (60%).

MS-CI: *m*/*z* = 206 (100%)[M + NH_4]$^+$, 189 (60%) [M + H]$^+$, 161 (27%).

HRMS (ES^+): *m*/*z* calcd for $C_{13}H_{16}O$ [M]$^+$, 189.1279; found, 189.1281.

31

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.94 (t, 3 H, *J* = 7.3 Hz, CH_3), 1.37 (s^6, 2 H, *J* = 7.4 Hz, CH$_3$C*H*$_2$), 1.59–1.66 (m, 2 H, CH$_3$CH$_2$C*H*$_2$), 2.68 [t, 2 H, *J* = 7.7 Hz, CH$_3$(CH$_2$)$_2$C*H*$_2$], 3.44 (t, 2 H, *J* = 6.9 Hz, CH_2Cl), 3.93 (t, 2 H, *J* = 6.9 Hz, COCH$_2$), 7.29 and 7.89 (2 × d, 4 H, *J* = 8.3 Hz, C_6H_4).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 14.3 (CH_3), 22.7 (CH$_3$C*H*$_2$), 33.5 (CH$_3$CH$_2$C*H*$_2$), 36.1 (CH$_2$Ar), 39.2 (CH_2), 41.6 (CH_2), 128.6 (Ar, CH), 129.1 (Ar, CH), 134.5 (Ar, C-1/4), 149.2 (Ar, C-1/4), 196.7 (CO).

MS-EI: *m*/*z* = 224 (5%) [M^+], 188 (6%), 161 (100%), 91 (40%).

MS-CI: *m*/*z* = 242 (90%) [M + NH_4]$^+$, 225 (20%) [M + H]$^+$, 221 (30%), 182 (75%).

HRMS (ES^+): *m*/*z* calcd for $C_{13}H_{18}ClO$ [M + H]$^+$, 225.1046; found, 225.1045.

3-Dimethylamino-1-(4-butylphenyl)propan-1-one (27)

To a soln of **29** (4.312 g, 19.2 mmol) and **31** (3.082 g, 16.4 mmol) in THF (30 mL), a soln of dimethylamine in THF (2 M, 58 mL, 3.2 equiv) was added dropwise at 0 °C. The reaction mixture was stirred for 24 h at r.t. The THF was evaporated under reduced pressure. HCl (2 M, 60 mL) was cautiously added followed by an extraction with $CHCl_3$ (3 × 75 mL). The organic extracts were dried over anhyd $MgSO_4$. Following filtration, the $CHCl_3$ was removed in vacuo to yield **27** as its hydrochloride salt (6.998 g, 73%) as an orange powder.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.86 (t, 3 H, *J* = 7.3 Hz, CH_3), 1.28 (s^6, 2 H, *J* = 7.4 Hz, CH$_3$C*H*$_2$), 1.53 (q^5, 2 H, *J* = 7.6 Hz, CH$_3$CH$_2$C*H*$_2$), 2.61 [t, 2 H, *J* = 7.8 Hz, CH$_3$(CH$_2$)$_2$C*H*$_2$], 2.79 [d, 6 H, *J* = 4.8 Hz, N(CH$_3$)$_2$], 3.46 (dt, 2 H, *J* = 4.8, 7.0 Hz, CH$_2$N), 3.65 (t, 2 H, *J* = 7.0 Hz, COCH$_2$), 7.20 and 7.83 (2 × d, 4 H, *J* = 8.3 Hz, C_6H_4), 12.44 (br s, 1 H, HCl).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 14.3 (CH_3), 22.7 (CH$_3$C*H*$_2$), 33.5 (CH$_3$CH$_2$C*H*$_2$), 34.1 (CO*C*H$_2$), 36.1 (CH$_2$Ar), 43.7 (NCH$_3$), 53.1 (CH$_2$N), 128.8 (Ar, CH), 129.2 (Ar, CH), 133.6 (Ar, C-1/4), 150.5 (Ar, C-1/4), 195.8 (CO).

MS-EI: *m*/*z* =233 (4%) [M^+], 188 (11%), 161 (38%), 117 (13%), 91 (28%).

MS-CI: *m*/*z* =234 (45%) [M + H]$^+$, 208 (42%), 192 (34%), 162 (10%).

HRMS (ES^+): *m*/*z* calcd for $C_{15}H_{24}NO$ [M + H]$^+$, 234.1858; found, 234.1856.

***N*,*N*-Dimethyl-3-(4-butylphenyl)propylamine (33)**

To a stirred soln of **27** (8.276 g, 30.8 mmol) in EtOH (100 mL), was added 10% Pd/C (0.800 g). Hydrogenation was carried out at atmospheric pressure and 50 °C with almost the theoretical number of moles of H_2 being adsorbed. The catalyst was removed by suction filtration (using celite as a filter aid) and EtOH was removed in vacuo to yield the hydrochloride salt of **33** (7.461 g, 95%) as an orange powder.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.85 (t, 3 H, *J* = 7.3 Hz, CH_3), 1.27 (s^6, 2 H, *J* = 7.4 Hz, CH$_3$C*H*$_2$), 1.45–1.54 (m, 2 H, CH$_3$CH$_2$C*H*$_2$), 2.05–2.15 (m, 2 H, C*H*$_2$CH$_2$N), 2.61 [t, 2 H, *J* = 7.3 Hz, C*H*$_2$(CH$_2$)$_2$N], 2.50 [t, 2 H, *J* = 7.7 Hz, CH$_3$(CH$_2$)$_2$C*H*$_2$], 2.69 [s, 6 H, N(CH$_3$)$_2$], 2.87–2.91 (m, 2 H, CH$_2$N), 6.99 and 7.03 (2 × d, 4 H, *J* = 8.3 Hz, C_6H_4), 12.10 (br s, 1 H, HCl).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 14.4 (CH_3), 22.7 (CH$_3$C*H*$_2$), 26.0 (*C*H$_2$CH$_2$N), 32.5 (CH$_3$CH$_2$C*H*$_2$), 34.0 (ArC*H*$_2$), 35.7 (CH$_2$Ar), 43.2

(NCH_3), 57.7 (CH_2N), 128.5 (Ar, CH), 129.2 (Ar, CH), 136.8 (Ar, C-1/4), 141.7 (Ar, C-1/4).

The hydrochloride (7.411 g, 29.1 mmol) was quenched with a sat. aq Na_2CO_3 until a pH of ~10 was reached (confirmed by indicator paper). Extraction with EtOAc (3 × 50 mL) and removal of the solvent in vacuo yielded **33** (6.301 g, 99%) as a brown oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.84 (t, 3 H, *J* = 7.3 Hz, CH_3), 1.28 (s^6, 2 H, *J* = 7.3 Hz, CH_3CH_2), 1.47–1.55 (m, 2 H, $CH_3CH_2CH_2$), 1.66–1.76 (m, 2 H, CH_2CH_2N), 2.14 [s, 6 H, $N(CH_3)_2$], 2.19–2.24 (m, 2 H, CH_2N), 2.49 (t, 2 H, *J* = 8.0 Hz, $ArCH_2$), 2.51 (t, 2 H, *J* = 8.1 Hz, $ArCH_2$), 7.07 and 7.20 (2 × d, 4 H, *J* = 8.0 Hz, C_6H_4).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 14.4 (CH_3), 22.8 (CH_3CH_2), 29.9 (CH_2CH_2N), 33.7 ($CH_3CH_2CH_2$), 34.2 ($ArCH_2$), 35.7 (CH_2Ar), 45.9 (NCH_3), 59.8 (CH_2N), 128.6 (Ar, CH), 128.7 (Ar, CH), 139.8 (Ar, C-1/4), 142.8 (Ar, C-1/4).

MS-EI: *m*/*z* = 219 (24%) [M^+], 131 (33%), 117 (25%), 115 (21%), 91 (26%).

MS-CI: *m*/*z* = 220 (100%) $[M + H]^+$, 206 (7%).

HRMS: *m*/*z* calcd for $C_{15}H_{25}N$ [M^+], 219.1987; found, 219.1986.

N-[3-(4-Butylphenyl)propyl]-*N*,*N*-dimethyl-3-ammonio-1-propanesulfonate (11)

To a stirred soln of 1,3-propanesultone (1.961 g, 16.1 mmol) in EtOAc (30 mL), was added a soln of **33** (3.136 g, 14.3 mmol) in EtOAc (30 mL). The reaction mixture was stirred for 253 h at r.t. The resulting white precipitate was filtered, washed with Et_2O, and dried in vacuo to yield **11** (2.097 g, 43%) as an off-white crystalline solid.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.95 (t, 3 H, *J* = 7.4 Hz, CH_3), 1.36 (s^6, 2 H, *J* = 7.3 Hz, CH_3CH_2), 1.59 (q^5, 2 H, *J* = 7.6 Hz, $CH_3CH_2CH_2$), 2.08–2.24 (m, 4 H, $CH_2CH_2SO_3$ and CH_2CH_2N), 2.59 (t, 2 H, *J* = 7.7 Hz, $ArCH_2$), 2.70 (t, 2 H, *J* = 7.5 Hz, $ArCH_2$), 2.88 (t, 2 H, *J* = 6.8 Hz, CH_2SO_3), 3.09 [s, 6 H, $N(CH_3)_2$], 3.31–3.36 (m, 2 H, CH_2N), 3.52 (m, 2 H, NCH_2), 7.14 and 7.20 (2 × d, 4 H, *J* = 8.1 Hz, C_6H_4).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 14.7 (CH_3), 20.3 (NCH_2CH_2), 23.7 (CH_3CH_2), 25.7 (CH_2CH_2N), 33.2 ($CH_3CH_2CH_2$), 35.5 (CH_2Ar), 36.6 ($ArCH_2$), 49.0 (CH_2SO_3), 51.7 (NCH_3), 64.1 (NCH_2), 65.4 (CH_2N), 129.8 (Ar, CH), 130.2 (Ar, CH), 138.8 (Ar, C-1/4), 142.6 (Ar, C-1/4).

(MS-ES^+): *m*/*z* = 683 (8%) $[2M + H]^+$, 577 (10%), 358 (19%), 342 (100%) $[M + H]^+$, 236 (93%), 220 (38%).

(MS-ES^-): *m*/*z* = 741 (7%) $[2M + AcO]^-$, 416 (45%), 400 (100%) $[M + AcO]^-$, 301 (11%), 166 (24%), 130 (22%).

HRMS (ES^+): *m*/*z* calcd for $C_{18}H_{32}NSO_3$ $[M + H]^+$, 342.2103; found, 342.2100.

N-[3-(4-Hexylphenyl)propyl]-*N*,*N*-dimethyl-3-ammonio-1-propanesulfonate (12)

1-(4-Hexylphenyl)propenone (30), 3-Chloro-1-(4-hexylphenyl)-propan-1-one (**32**)

To a suspension of $AlCl_3$ (9.842 g, 74.0 mmol) in anhyd 1,2 dichloroethane (30 mL) at 0 °C under N_2 was added acryloyl chloride (3.7 mL, 4.122 g, 45.3 mmol) in anhyd dichloroethane (20 mL). A soln of 1-phenylhexane (7.0 mL, 6.027 g, 37.2 mmol) in dichloroethane (30 mL) was added dropwise to the resulting stirred mixture. After stirring in the dark for 6.75 h at r.t., the reaction mixture was poured into a mixture of ice H_2O (50 mL), HCl (12 N, 50 mL) and extracted with CH_2Cl_2 (3 × 100 mL). The combined organic extracts were washed with sat. aq $NaHCO_3$ (3 × 100 mL), brine (2 × 100 mL), and dried over anhyd $MgSO_4$. The filtered soln was evaporated in vacuo to yield **30** (1.668 g, 7.7 mmol) and **32** (4.324 g, 17.2 mmol) in 67% yield (31:69 respectively) as a pale yellow powder.

30

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.81 (t, 3 H, *J* = 6.9 Hz, CH_3), 1.16–1.29 [m, 6 H, $CH_3(CH_2)_3$], 1.55 [q^5, 2 H, *J* = 6.7 Hz, $CH_3(CH_2)_3CH_2$], 2.59 [t, 2 H, *J* = 6.3 Hz, $CH_3(CH_2)_4CH_2$], 5.83 (dd, 1 H, *J* = 1.8, 10.5 Hz, CH=CH*H*), 6.36 (dd, 1 H, *J* = 1.8, 17.1 Hz, CH=CH*H*), 7.10 (dd, 1 H, *J* = 10.5, 17.1 Hz, C*H*=CH_2), 7.20 and 7.80 (2 × d, 4 H, *J* = 8.3 Hz, C_6H_4).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 14.3 (CH_3), 22.9 (CH_3CH_2), 29.3 (CH_2), 29.7 (CH_2), 32.0 (CH_2), 36.4 (CH_2Ar), 129.0 (Ar, CH), 129.1 (Ar, CH), 129.8 (CH_2), 132.9 (CH), 135.4 (Ar, C-1/4), 149.7 (Ar, C-1/4), 190.9 (CO).

MS-EI: *m*/*z* = 216 (7%) [M^+], 189 (100%), 91 (22%).

MS-CI: *m*/*z* = 234 (100%) $[M + NH_4]^+$, 217 (73%) $[M + H]^+$, 189 (41%), 90 (46%).

HRMS: *m*/*z* calcd for $C_{15}H_{20}O$ $[M]^+$, 216.1514; found, 216.1517.

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^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.81 (t, 3 H, *J* = 6.9 Hz, CH_3), 1.16–1.29 [m, 6 H, $CH_3(CH_2)_3$], 1.55 [q^5, 2 H, *J* = 6.7 Hz, $CH_3(CH_2)_3CH_2$], 2.59 [t, 2 H, *J* = 6.3 Hz, $CH_3(CH_2)_4CH_2$], 3.37 (t, 2 H, *J* = 6.9 Hz, CH_2Cl), 3.85 (t, 2 H, *J* = 6.9 Hz, $COCH_2$), 7.20 and 7.80 (2 × d, 4 H, *J* = 8.3 Hz, C_6H_4).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 14.3 (CH_3), 22.9 (CH_3CH_2), 29.3, 29.7, 32.0 (3 × CH_2), 36.4 (CH_2Ar), 39.2, 41.6 (2 × CH_2), 128.6 (Ar, CH), 129.0 (Ar, CH), 134.6 (Ar, C-1/4), 149.1 (Ar, C-1/4), 196.7 (CO).

MS-EI: *m*/*z* = 252 (3%) [M^+], 189 (100%), 91 (22%).

MS-CI: *m*/*z* = 272 (25%) $[M + NH_4]^+$, 253 (18%) $[M + H]^+$, 189 (41%), 90 (46%).

HRMS: *m*/*z* calcd for $C_{15}H_{21}ClO$ $[M]^+$, 252.1281; found, 252.1277.

3-Dimethylamino-1-(4-hexylphenyl)propan-1-one (28)

To a soln of **30** (1.642 g, 7.6 mmol) and **32** (4.284 g, 17.0 mmol) in THF (30 mL), a soln of dimethylamine in THF (2 M, 60 mL) was added dropwise at 0 °C. The reaction mixture was stirred for 24 h at r.t. The THF was evaporated under reduced pressure. HCl (2 M, 60 mL) was cautiously added followed by extraction with $CHCl_3$ (3 × 75 mL) and drying over anhyd $MgSO_4$. Following filtration, the $CHCl_3$ was removed in vacuo to yield **28** as its hydrochloride salt (6.032 g, 83%) as a yellow/orange powder.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.81 (t, 3 H, *J* = 6.8 Hz, CH_3), 1.15–1.36 [m, 6 H, $CH_3(CH_2)_3$], 1.55 [q^5, 2 H, *J* = 7.6 Hz, $CH_3(CH_2)_3CH_2$], 2.60 [t, 2 H, *J* = 7.7 Hz, $CH_3(CH_2)_4CH_2$], 2.78 [s, 6 H, $N(CH_3)_2$], 3.45 (t, 2 H, *J* = 6.8 Hz, $COCH_2$), 3.65 (t, 2 H, *J* = 6.9 Hz, CH_2N), 7.20 and 7.83 (2 × d, 4 H, *J* = 8.2 Hz, C_6H_4), 12.57 (br s, 1 H, HCl).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 13.1 (CH_3), 21.5 (CH_3CH_2), 27.9 (CH_2), 30.0 (CH_2), 30.6 (CH_2), 32.7 ($COCH_2$), 35.0 (CH_2Ar), 42.3 (NCH_3), 51.7 (CH_2N), 127.4 (Ar, CH), 127.9 (Ar, CH), 132.1 (Ar, C-1/4), 149.2 (Ar, C-1/4), 194.4 (CO).

MS-EI: *m*/*z* = 261 (100%) [M^+].

MS-CI: *m*/*z* = 262 (37%) $[M + H]^+$, 234 (18%), 217 (76%), 189 (20%).

HRMS: *m*/*z* calcd for $C_{17}H_{27}NO$ $[M]^+$, 261.2093; found, 261.2092.

N,*N*-Dimethyl-3-(4-hexylphenyl)propylamine (34)

To a stirred soln of **28** (5.982 g, 20.1 mmol) in EtOH (100 mL), was added 10% Pd/C (0.600 g). Hydrogenation was carried out at atmospheric pressure and 50 °C with almost the theoretical number of

moles of H_2 being adsorbed. The catalyst was removed by suction filtration (using celite as a filter aid) and EtOH was removed in vacuo to yield the hydrochloride salt of **34** (5.404 g, 95%) as an orange powder.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.89 (t, 3 H, *J* = 6.4 Hz, CH_3), 1.26–1.40 [m, 6 H, $CH_3(CH_2)_3$], 1.59 [q^5, 2 H, *J* = 7.1 Hz, $CH_3(CH_2)_3CH_2$], 2.18 (m, 2 H, CH_2CH_2N), 2.57 (t, 2 H, *J* = 7.7 Hz, $ArCH_2$), 2.70 (t, 2 H, *J* = 7.2 Hz, $ArCH_2$), 2.78 [s, 6 H, $N(CH_3)_2$], 2.96–2.99 (m, 2 H, CH_2N), 7.08 and 7.11 (2 × d, 4 H, *J* = 8.0 Hz, C_6H_4), 12.27 (br s, 1 H, HCl).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 14.5 (CH_3), 23.0 (CH_3CH_2), 26.0 (CH_2CH_2N), 29.4 (CH_2), 31.9 (CH_2), 32.1 (CH_2), 32.5 ($ArCH_2$), 35.9 (CH_2Ar), 43.3 (NCH_3), 57.8 (CH_2N), 128.6 (Ar, CH), 129.2 (Ar, CH), 136.7 (Ar, C-1/4), 141.7 (Ar, C-1/4).

MS-EI: *m*/*z* = 247 (100%) [M$^+$], 202 (18%), 189 (14%), 175 (16%).

MS-CI: *m*/*z* = 248 (100%) [M + H]$^+$, 131 (3%).

HRMS: *m*/*z* calcd for $C_{17}H_{29}N$ [M]$^+$, 247.2300; found, 247.2300.

The hydrochloride salt (5.310 g, 18.8 mmol) was quenched with a sat. aq Na_2CO_3 until a pH of ~10 was reached (confirmed by indicator paper). Extraction with EtOAc (3 × 50 mL) and removal of the solvent in vacuo yielded **34** (4.495 g, 97%) as a brown oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.81 (t, 3 H, *J* = 6.7 Hz, CH_3), 1.17–1.29 [m, 6 H, $CH_3(CH_2)_3$], 1.52 [q^5, 2 H, *J* = 7.5 Hz, $CH_3(CH_2)_3CH_2$], 1.71 (q^5, 2 H, *J* = 7.7 Hz, CH_2CH_2N), 2.15 [s, 6 H, $N(CH_3)_2$], 2.23 (t, 2 H, *J* = 7.5 Hz, CH_2N), 2.49 (t, 2 H, *J* = 7.9 Hz, $ArCH_2$), 2.52 (t, 2 H, *J* = 7.7 Hz, $ArCH_2$), 7.02 (s, 4 H, C_6H_4).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 14.5 (CH_3), 23.0 (CH_3CH_2), 29.9 (CH_2CH_2N), 30.0 (CH_2), 32.0 (CH_2), 33.0 (CH_2), 33.7 ($ArCH_2$), 36.0 (CH_2Ar), 45.9 (NCH_3), 59.8 (CH_2N), 128.6 (Ar, CH), 128.7 (Ar, CH), 139.8 (Ar, C-1/4), 140.7 (Ar, C-1/4).

N-[3-(4-Hexylphenyl)propyl]-*N*,*N*-dimethyl-3-ammonio-1-propanesulfonate (12)

Prepared using the procedure described above starting from **34** (2.090 g, 8.5 mmol). The product **12** was obtained as an off-white crystalline solid (1.286 g, 41%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.89 (t, 3 H, *J* = 6.7 Hz, CH_3), 1.30–1.34 [m, 6 H, $CH_3(CH_2)_3$], 1.58 [q^5, 2 H, *J* = 7.3 Hz, $CH_3(CH_2)_3CH_2$], 2.06–2.17 (m, 4 H, $CH_2CH_2SO_3$ and CH_2CH_2N), 2.56 (t, 2 H, *J* = 7.4 Hz, $ArCH_2$), 2.68 (t, 2 H, *J* = 7.5 Hz, $ArCH_2$), 2.86 (t, 2 H, *J* = 6.8 Hz, CH_2SO_3), 3.07 [s, 6 H, $N(CH_3)_2$], 3.28–3.34 (m, 2 H, CH_2N), 3.50 (m, 2 H, NCH_2), 7.11 and 7.17 (2 × d, 4 H, *J* = 8.1 Hz, C_6H_4).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 14.4 (CH_3), 19.8 (NCH_2CH_2), 23.7 (CH_3CH_2), 25.3 (CH_2CH_2N), 30.0 (CH_2), 32.8 (CH_2), 32.8 (CH_2), 32.9 ($ArCH_2$), 36.5 (CH_2Ar), 48.6 (CH_2SO_3), 51.3 (NCH_3), 63.7 (NCH_2), 65.0 (CH_2N), 129.4 (Ar, CH), 129.7 (Ar, CH), 138.4 (Ar, C-1/4), 142.2 (Ar, C-1/4).

(MS-ES$^+$): *m*/*z* = 761 (2%) [2M + Na]$^+$, 739 (10%) [2M + H]$^+$, 392 (11%) [M + Na]$^+$, 370 (100%) [M + H]$^+$, 248 (13%).

(MS-ES$^-$): *m*/*z* = 797 (8%) [2M + AcO]$^-$, 526 (8%), 428 (100%) [M + AcO]$^-$, 404 (8%) [M + Cl]$^-$, 315 (15%), 157 (45%).

HRMS (ES$^+$): *m*/*z* calcd for $C_{20}H_{36}NSO_3$ [M + H]$^+$, 370.2416; found, 370.2420.

Butane Sulfobetaines 13–21

N-Hexyl-*N*,*N*-dimethyl-4-ammonio-1-butanesulfonate (13)

To a stirred soln of 1,4-butanesultone (8.941 g, 65.7 mmol) in EtOAc (30 mL), was added *N*,*N*-dimethylhexylamine (9.470 g, 73.4 mmol) in EtOAc (30 mL). The reaction mixture was stirred under reflux for 44 h. After cooling, the resulting white precipitate was filtered, washed with Et_2O, and dried in vacuo to yield **13** (10.906 g, 63%) as a white crystalline solid; mp 260–262 °C.

^{1}H NMR (400 MHz, CD_3OD): δ = 0.90–0.96 (m, 3 H, CH_3), 1.34–1.41 [m, 6 H, $CH_3(CH_2)_3$], 1.79 (m, 2 H, CH_2CH_2N), 1.84 (q^5, 2 H, *J* = 7.1 Hz, $CH_2CH_2SO_3$), 1.90–1.99 (m, 2 H, NCH_2CH_2), 2.89 (t, 2 H, *J* = 7.1 Hz, CH_2SO_3), 3.07 [s, 6 H, $N(CH_3)_2$], 3.29 (m, 2 H, CH_2N), 3.34 (m, 2 H, NCH_2).

^{13}C NMR (101 MHz, CD_3OD): δ = 14.4 (CH_3), 22.3, 23.0, 23.5 (3 × CH_2), 23.5 ($CH_2CH_2SO_3$), 27.1 (NCH_2CH_2), 32.4 (CH_2CH_2N), 51.2 (NCH_3), 51.3 (CH_2SO_3), 64.9 (NCH_2), 65.6 (CH_2N).

MS-EI: *m*/*z* = 265 (2%) [M$^+$], 264 (15%) [M–H]$^+$, 194 (40%), 180 (20%), 137 (30%), 129 (100%), 128 (80%).

MS-CI: *m*/*z* = 266 [M + H]$^+$, 2%), 252 (3%), 170 (7%), 168 (4%), 154 (79%), 131 (13%), 130 (100%).

HRMS: *m*/*z* calcd for $C_{12}H_{28}NSO_3$ [M + H]$^+$, 266.1790; found, 266.1788.

N-Heptyl-*N*,*N*-dimethyl-4-ammonio-1-butanesulfonate (14)

Prepared using the procedure described above starting from *N*,*N*-dimethylheptylamine (9.545 g, 66.7 mmol). The product **14** was obtained as a white crystalline solid (13.566 g, 73%); mp 252–253 °C.

^{1}H NMR (400 MHz, CD_3OD): δ = 0.81 (t, 3 H, *J* = 6.8 Hz, CH_3), 1.20–1.30 [m, 8 H, $CH_3(CH_2)_4$], 1.61–1.68 (m, 2 H, CH_2CH_2N), 1.72 (q^5, 2 H, *J* = 7.2 Hz, $CH_2CH_2SO_3$), 1.79–1.86 (m, 2 H, NCH_2CH_2), 2.76 (t, 2 H, *J* = 7.2 Hz, CH_2SO_3), 2.95 [s, 6 H, $N(CH_3)_2$], 3.18 (m, 2 H, CH_2N), 3.23 (m, 2 H, NCH_2).

^{13}C NMR (101 MHz, CD_3OD): δ = 14.3 (CH_3), 22.3 (CH_2), 23.0 (CH_2), 23.5 (CH_2), 23.5 ($CH_2CH_2SO_3$), 27.3 (NCH_2CH_2), 29.9 (CH_2), 32.7 (CH_2CH_2N), 51.0 (NCH_3), 51.1 (CH_2SO_3), 64.8 (NCH_2), 65.4 (CH_2N).

MS-EI: *m*/*z* = 279 (1%) [M$^+$], 278 (2%) [M – H]$^+$, 194 (5%), 180 (5%), 144 (18%), 143 (100%), 142 (30%).

MS-CI: *m*/*z* = 280 (2%) [M + H]$^+$, 266 (1%), 196 (2%), 184 (11%), 154 (59%), 144 (100%), 130 (33%).

HRMS: *m*/*z* calcd for $C_{13}H_{30}NSO_3$ [M + H]$^+$, 280.1946; found, 280.1942.

N-Octyl-*N*,*N*-dimethyl-4-ammonio-1-butanesulfonate (15)

To a stirred soln of 1,4-butanesultone (7.696 g, 56.6 mmol) in EtOAc (20 mL), was added a soln of *N*,*N*-dimethyloctylamine (8.881 g, 56.6 mmol) in EtOAc (20 mL). The reaction mixture was stirred under reflux for 2.5 h. After cooling, the resulting white precipitate was filtered, washed with Et_2O, and dried in vacuo yielding **15** (10.465 g, 63%) as a white crystalline solid; mp 251–252 °C.

^{1}H NMR (400 MHz, CD_3OD): δ = 0.81 (t, 3 H, *J* = 6.8 Hz, CH_3), 1.18–1.32 [m, 10 H, $CH_3(CH_2)_5$], 1.62–1.70 (m, 2 H, CH_2CH_2N), 1.73 (q^5, 2 H, J = 7.2 Hz, $CH_2CH_2SO_3$), 1.80–1.88 (m, 2 H, NCH_2CH_2), 2.78 (t, 2 H, *J* = 7.2 Hz, CH_2SO_3), 2.98 [s, 6 H, $N(CH_3)_2$], 3.20 (m, 2 H, CH_2N), 3.25 (m, 2 H, NCH_2).

^{13}C NMR (101 MHz, CD_3OD): δ = 14.4 (CH_3), 22.3 (CH_2), 23.0 (CH_2), 23.5 (CH_2), 23.6 ($CH_2CH_2SO_3$), 27.4 (NCH_2CH_2), 30.2 (CH_2), 30.2 (CH_2), 32.8 (CH_2CH_2N), 51.1 (NCH_3), 51.4 (CH_2SO_3), 64.8 (NCH_2), 65.4 (CH_2N).

MS-EI: *m*/*z* = 293 (1%) [M$^+$], 292 (32%) [M – H]$^+$, 280 (8%), 194 (34%), 180 (50%), 156 (100%).

MS-CI: *m*/*z* = 294 (3%) [M + H]$^+$, 280 (4%), 198 (15%), 196 (10%), 158 (100%), 154 (54%), 144 (34%).

HRMS: *m*/*z* calcd for $C_{14}H_{32}NSO_3$ [M + H]$^+$, 294.2103; found, 294.2100.

***N*-Benzyl-*N*,*N*-dimethyl-4-ammonio-1-butanesulfonate (16)**

To a stirred soln of 1,4-butanesultone (6.270 g, 46.1 mmol) in EtOAc (70 mL), was added *N*,*N*-dimethylbenzylamine (6.400 g, 40.8 mmol) in EtOAc (70 mL). The reaction mixture was stirred under reflux for 48 h. After cooling, the resulting white precipitate was filtered, washed with Et_2O, and dried in vacuo to yield **16** (4.875 g, 44%) as a white crystalline solid; mp 262–264 °C (lit.[3] mp 285–286 °C).

^{1}H NMR (400 MHz, CD_3OD): δ = 1.85 [q[5], 2 H, *J* = 7.5 Hz, $CH_2(CH_2)_2SO_3$], 2.08 (m, 2 H, $CH_2CH_2SO_3$), 2.90 (t, 2 H, *J* = 6.9 Hz, CH_2SO_3), 3.02 [s, 6 H, $N(CH_3)_2$], 3.36 (m, 2 H, NCH_2), 4.53 (s, 2 H, $PhCH_2N$), 7.50–7.60 (m, 5 H, C_6H_5).

^{13}C NMR (101 MHz, CD_3OD): δ = 22.4 (NCH_2CH_2), 23.0 ($CH_2CH_2SO_3$), 50.3 (NCH_3), 51.3 (CH_2SO_3), 65.2 (NCH_2), 68.7 (CH_2N), 128.9 (Ph, C-1), 130.3 (Ph, CH), 131.8 (Ph, CH), 134.1 (Ph, CH).

(MS-ES$^+$): *m*/*z* = 565 (28%) [2 M + Na]$^+$, 543 (8%) [2 M + H]$^+$, 294 (100%) [M + Na]$^+$, 272 (47%) [M + H]$^+$.

(MS-ES$^-$): 346 (60%), 316 (63%), 270 (100%) [M − H]$^-$.

HRMS (ES$^+$): *m*/*z* calcd for $C_{13}H_{30}NSO_3$ [M + H]$^+$, 272.1320; found, 272.1322.

***N*-Phenylethyl-*N*,*N*-dimethyl-4-ammonio-1-butanesulfonate (17)**

To a stirred soln of 1,4-butanesultone (5.607 g, 41.2 mmol) in EtOAc (50 mL), was added *N*,*N*-dimethylphenethylamine (6.215 g, 41.7 mmol) in EtOAc (50 mL). The reaction mixture was stirred under reflux for 117 h. After cooling, the resulting white precipitate was filtered, washed with Et_2O, and dried in vacuo to yield **17** (5.951 g, 51%) as a white crystalline solid; mp 277–278 °C (lit.[3] mp 274–275 °C).

^{1}H NMR (400 MHz, CD_3OD): δ = 1.84 [q[5], 2 H, *J* = 7.3 Hz, $CH_2(CH_2)_2SO_3$], 1.98 (m, 2 H, $CH_2CH_2SO_3$), 2.88 (t, 2 H, *J* = 7.2 Hz, CH_2SO_3), 3.08–3.13 (m, 2 H, $PhCH_2$), 3.16 [s, 6 H, $N(CH_3)_2$], 3.42 (m, 2 H, NCH_2), 3.52 (m, 2 H, CH_2N), 7.24–7.36 (m, 5 H, C_6H_5).

^{13}C NMR (101 MHz, CD_3OD): δ = 22.3 (NCH_2CH_2), 23.0 ($CH_2CH_2SO_3$), 29.8 ($ArCH_2$), 51.2 (CH_2SO_3), 51.3 (NCH_3), 64.9 (NCH_2), 66.1 (CH_2N),128.3 (Ph, CH), 129.9 (Ph, CH), 130.1 (Ph, CH), 137.1 (Ph, C-1).

MS-EI: *m*/*z* = 285 (18%) [M$^+$], 284 (100%) [M – H]$^+$, 231 (50%).

MS-CI: *m*/*z* = 286 (64%) [M + H]$^+$, 272 (100%).

HRMS (ES$^+$): *m*/*z* calcd for $C_{14}H_{32}NSO_3$ [M + H]$^+$, 286.1477; found, 286.1481.

***N*-Phenylpropyl-*N*,*N*-dimethyl-4-ammonio-1-butanesulfonate (18)**

To a stirred soln of 1,4-butanesultone (2.180 g, 16.0 mmol) in EtOAc (20 mL), was added a soln of **24** (1.408 g, 8.6 mmol) in EtOAc (20 mL). The reaction mixture was stirred under reflux for 156 h. After cooling, the resulting white precipitate was filtered, washed with Et_2O, and dried in vacuo to yield **18** (1.390 g, 54%) as a white crystalline solid; mp 261–262 °C.

^{1}H NMR (400 MHz, CD_3OD): δ = 1.77–1.83 [m, 4 H, $(CH_2)_2CH_2SO_3$], 2.03–2.15 (m, 2 H, $PhCH_2CH_2$), 2.71 (t, 2 H, *J* = 7.5 Hz, CH_2SO_3), 2.84 (t, 2 H, *J* = 6.8 Hz, $PhCH_2$), 3.05 (s, 6 H, $N(CH_3)_2$), 3.27–3.34 (m, 4 H, CH_2NCH_2), 7.19–7.32 (m, 5 H, C_6H_5).

^{13}C NMR (101 MHz, CD_3OD): δ = 22.2 (NCH_2CH_2), 22.9 ($CH_2CH_2SO_3$), 25.3 (CH_2CH_2N), 33.1 ($ArCH_2$), 51.2 (CH_2SO_3), 51.3 (NCH_3), 64.7 (NCH_2), 64.7 (CH_2N), 127.5 (Ph, CH), 129.5 (Ph, CH), 129.7 (Ph, CH), 141.3 (Ph, C-1).

MS-EI: *m*/*z* = 299 (40%) [M$^+$], 298 (100%) [M – H]$^+$, 254 (24%), 246 (28%).

MS-CI: *m*/*z* = 300 (58%) [M + H]$^+$, 268 (44%), 252 (100%), 238 (55%), 222 (53%).

HRMS (ES$^+$): *m*/*z* calcd for $C_{15}H_{26}NSO_3$ [M + H]$^+$, 300.1633; found, 300.1634.

***N*-Phenylbutyl-*N*,*N*-dimethyl-4-ammonio-1-butanesulfonate (19)**

To a stirred soln of 1,4-butanesultone (1.000 g, 7.4 mmol) in EtOAc (25 mL), was added a soln of **25** (1.126 g, 6.9 mmol) in EtOAc (25 mL). The reaction mixture was stirred under reflux for 164 h. After cooling, the resulting white precipitate was filtered, washed with Et_2O, and dried in vacuo to yield **19** (0.618 g, 29%) as a white crystalline solid; mp 243–246 °C.

^{1}H NMR (250 MHz, CD_3OD): δ = 1.67–1.94 [m, 8 H, $PhCH_2(CH_2)_2$ and $(CH_2)_2CH_2SO_3$], 2.71 (t, 2 H, *J* = 7.2 Hz, $PhCH_2$), 2.86 (t, 2 H, *J* = 7.0 Hz, CH_2SO_3), 3.04 [s, 6 H, $N(CH_3)_2$], 3.27–3.33 (m, 4 H, CH_2NCH_2), 7.17–7.28 (m, 5 H, C_6H_5).

^{13}C NMR (63 MHz, CD_3OD): δ = 22.3 (NCH_2CH_2), 22.9 ($ArCH_2CH_2$), 23.0 ($CH_2CH_2SO_3$), 29.1 (CH_2CH_2N), 36.0 ($ArCH_2$), 51.2 (NCH_3), 51.3 (CH_2SO_3), 64.8 (NCH_2), 65.2 (CH_2N), 127.1 (Ph, CH), 129.5 (Ph, CH), 129.5 (Ph, CH), 142.8 (Ph, C-1).

MS-EI: *m*/*z* = 313 (54%) [M$^+$], 312 (100%) [M – H]$^+$, 234 (60%), 218 (99%).

MS-CI: *m*/*z* = 314 (66%) [M + H]$^+$, 300 (100%).

HRMS (ES$^+$): *m*/*z* calcd for $C_{16}H_{28}NSO_3$ [M + H]$^+$, 314.1790; found, 314.1787.

***N*-[3-(4-Butylphenyl)propyl]-*N*,*N*-dimethyl-4-ammonio-1-butanesulfonate (20)**

To a stirred soln of 1,4-butanesultone (2.186 g, 16.1 mmol) in EtOAc (30 mL), was added a soln of **33** (3.136 g, 14.3 mmol) in EtOAc (30 mL). The reaction mixture was stirred under reflux for 253 h. After cooling, the resulting white precipitate was filtered, washed with Et_2O and dried in vacuo to yield **20** (1.980 g, 39%) as an off-white crystalline solid; mp 202–204 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.93 (t, 3 H, *J* = 7.3 Hz, CH_3), 1.34 (s[6], 2 H, *J* = 7.4 Hz, CH_3CH_2), 1.57 (q[5], 2 H, *J* = 7.6 Hz, $CH_3CH_2CH_2$), 1.78–1.90 [m, 4 H, $(CH_2)_2CH_2SO_3$], 2.01–2.17 (m, 2 H, CH_2CH_2N), 2.58 (t, 2 H, *J* = 7.7 Hz, $ArCH_2$), 2.67 (t, 2 H, *J* = 7.4 Hz, $ArCH_2$), 2.85 (t, 2 H, *J* = 6.6 Hz, CH_2SO_3), 3.04 [s, 6 H, $N(CH_3)_2$], 3.27–3.35 (m, 4 H, NCH_2), 7.12 and 7.17 (2 × d, 2 H, *J* = 8.0 Hz, C_6H_4).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 14.3 (CH_3), 22.2 (NCH_2CH_2), 23.0 ($CH_2CH_2SO_3$), 23.3 (CH_3CH_2), 25.4 (CH_2CH_2N), 32.7 ($CH_3CH_2CH_2$), 35.0 (CH_2Ar), 36.2 ($ArCH_2$), 51.3 (CH_2SO_3), 51.3 (NCH_3), 64.7 (NCH_2), 65.8 (CH_2N), 129.4 (Ar, CH), 129.8 (Ar, CH), 138.5 (Ar, C-1/4), 141.2 (Ar, C-1/4).

(MS-ES$^+$): *m*/*z* = 711 (10%) [2 M + H]$^+$, 372 (7%), 356 (100%) [M + H]$^+$.

(MS-ES$^-$): *m*/*z* = 769 (6%) [2 M + AcO]$^-$, 430 (45%), 414 (100%) [M + AcO]$^-$, 180 (20%).

HRMS (ES$^+$): *m*/*z* calcd for $C_{19}H_{34}NSO_3$ [M + H]$^+$, 356.2259; found, 356.2263.

***N*-[3-(4-Hexylphenyl)propyl]-*N*,*N*-dimethyl-4-ammonio-1-butanesulfonate (21)**

Prepared using the procedure described in 4.9.8 starting from **34** (2.090 g, 8.5 mmol). The product **21** was obtained as an off-white crystalline solid (1.237 g, 38%); mp 219–221 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.89 (t, 3 H, *J* = 6.5 Hz, CH_3), 1.27–1.38 [m, 6 H, $CH_3(CH_2)_3$], 1.54–1.62 [m, 2 H, $CH_3(CH_2)_3CH_2$], 1.75–1.91 [m, 4 H, $(CH_2)_2CH_2SO_3$], 2.03–2.20 (m, 2 H, CH_2CH_2N), 2.57 (t, 2 H, *J* = 7.7 Hz, $ArCH_2$), 2.67 (t, 2 H, *J* = 7.4 Hz, $ArCH_2$), 2.84 (t, 2 H, *J* = 6.8 Hz, CH_2SO_3), 3.04 [s, 6 H, $N(CH_3)_2$], 3.27–3.34 (m, 4 H, NCH_2), 7.12 and 7.17 (2 × d, 4 H, *J* = 8.0 Hz, C_6H_4).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 14.4 (CH_3), 22.2 (NCH_2CH_2), 23.0 ($CH_2CH_2SO_3$), 23.7 (CH_3CH_2), 25.4 (CH_2CH_2N), 30.0 (CH_2), 32.8 (CH_2), 32.8 (CH_2), 32.9 ($ArCH_2$), 36.5 (CH_2Ar), 51.3 (CH_2SO_3), 51.3 (NCH_3), 64.6 (NCH_2), 64.8 (CH_2N), 129.4 (Ar, CH), 129.8 (Ar, CH), 138.5 (Ar, C-1/4), 142.3 (Ar, C-1/4).

(MS-ES$^+$): *m*/*z* = 789 (10%) $[2M + Na]^+$, 767 (10%) $[2M + H]^+$, 406 (11%) $[M + Na]^+$, 384 (100%) $[M + H]^+$.

(MS-ES$^-$): *m*/*z* = 825 (6%) $[2M + AcO]^-$, 442 (100%) $[M + AcO]^-$, 418 (7%) $[M + Cl]^-$, 363 (3%), 151 (13%).

HRMS (ES$^+$): *m*/*z* calcd for $C_{21}H_{38}NSO_3$ $[M + H]^+$, 384.2572; found, 384.2576.

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