Double-Chain Surfactants with Two Quaternary Ammonium Head Groups

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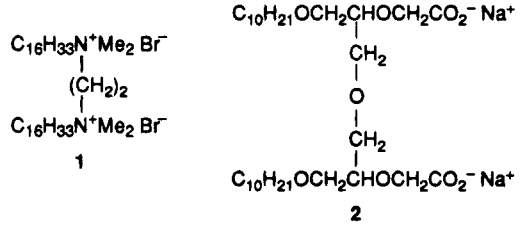
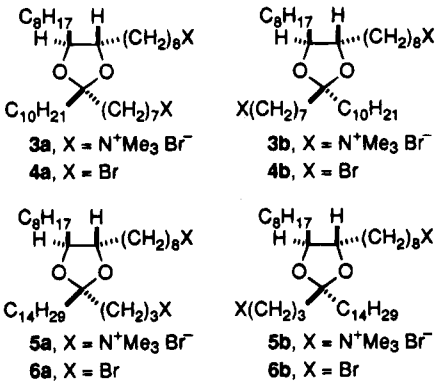
Double-chain surfactants with two head groups comprise an active research area.[3,4] Both dicationic[3] and dianionic[4] examples have been reported. Almost all of the former contain two quaternary ammonium units linked through the head groups (*e.g.*, **1**[3a]). Such bis-

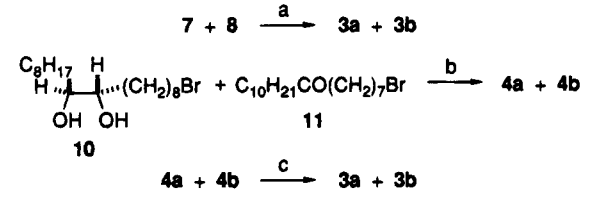


(quaternary ammonium) surfactants exhibit interesting solution behavior[3a-d] and bactericidal activity greater than that of single-chain quaternary ammonium surfactants.[3e] Dianionic double-chain surfactants contain carboxylate, phosphate, sulfate, and sulfonate head groups.[4] Generally, but not always,[4b] two long-chain anionic units are linked symmetrically at the α, γ, or ϵ positions with respect to the head groups (*e.g.*, **2**[4a]). The aggregate morphologies of double-chain, double-head group surfactants are of interest because the established relationship[5] between surfactant structure and morphology is not routinely applicable to them. Herein we report the synthesis and characterization of surfactants **3** and **5**.[6]



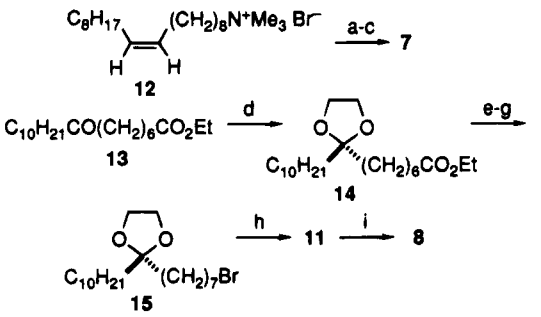
They represent two of only a few examples[3d] of double-chain, double-cationic head group surfactants wherein the linkage is between the alkyl chains and not the head groups. Surfactants **3** and **5** are isomers, differing only in the position of a ketal group linking two C18 chains bearing quaternary ammonium head groups, and each exists as a pair of diastereomers as illustrated. Also, **3** and **5** are second generation double-chain cleavable surfactants.[7] Such surfactants can be cleaved into two single-chain surfactants (eqs 1 and 2).

Scheme 1[a]

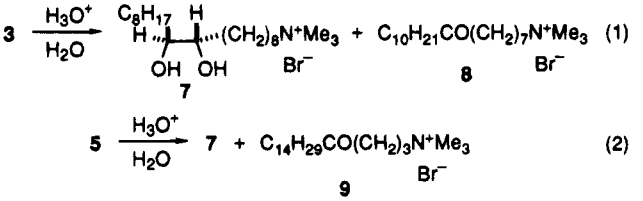


[a] Key: (a) *p*-$MeC_6H_4SO_3H$, 4 Å molecular sieves, CH_2Cl_2, 25 °C; (b) PPTS, C_6H_5Me, Dean-Stark; (c) Me_3N, MeOH, 25 °C.

Scheme 2[a]



[a] Key: (a) H_2O_2, HCO_2H; (b) KOH, H_2O; (c) HBr, H_2O; (d) $HOCH_2CH_2OH$, *p*-$MeC_6H_4SO_3H$, C_6H_6, Dean-Stark; (e) $LiAlH_4$, Et_2O; (f) $MeSO_2Cl$, Et_3N, CH_2Cl_2; (g) LiBr, THF; (h) HCl, H_2O, Me_2CO; (i) Me_3N, MeOH.



Surfactant **3** was prepared by the two routes of Scheme 1. In the first, the reaction of *vic*-diol surfactant **7** with keto surfactant **8** gave **3a** and **3b** directly. By reversed-phase HPLC the **3a/3b** ratio = 1.0. In the second route, the reaction of bromo diol **10** with bromo ketone **11** gave **4a** and **4a**, which were converted into **3a** and **3b**. By reversed-phase HPLC bromo ketals **4a** and **4b** were inseparable, and the resultant **3a/3b** ratio = 1.0.

Diol surfactant **7** was prepared by anti-hydroxylation of surfactant **12**,[8] and keto surfactant **8** from keto ester **13**[9] as outlined in Scheme 2. Bromo diol **10** was prepared from *vic*-diol acid **16**[10] as illustrated in Scheme 3.

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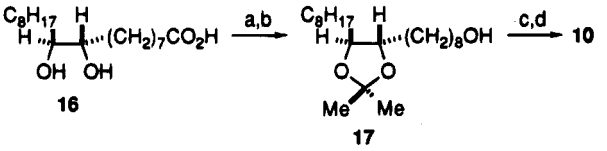
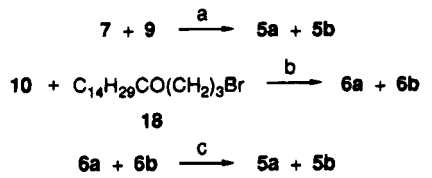
Scheme 3[a]



[a] Key: (a) Me_2CO, H_2SO_4; (b) $LiAlH_4$, Et_2O; (c) CBr_4, Bu_3P; (d) HBr, EtOH, H_2O.

Scheme 4[a]



[a] Key: (a) *p*-$MeC_6H_4SO_3H$, 4 Å molecular sieves, CH_2Cl_2, 25 °C; (b) PPTS, C_6H_5Me, Dean-Stark; (b) Me_3N, MeOH, 25 °C.

Surfactant **5** was prepared by the two routes of Scheme 4. In the first, the reaction of **7** with keto surfactant **9** gave **5a** and **5b** directly. By reversed-phase HPLC the **5a/5b** ratio = 1.0. In the second route, the reaction of **10** and **18** gave **6a** and **6b**, which were converted into **5a** and **5b**. By reversed-phase HPLC **6a** and **6b** were inseparable, and the resultant **5a/5b** ratio = 1.0. Keto surfactant **9** and bromo ketone **18** were prepared from methyl 4-oxooctadecanoate[11] with the procedures used for **8** and **11** in Scheme 2.

Surfactants **3** and **5** were characterized by dynamic laser light scattering (DLLS) measurements and their hydrolytic reactivities, and **3**, **5**, and **7-9** by critical micelle concentration (cmc) measurements.

DLLS measurements at 23 °C for **3** were made in 0.10 M NaBr and in a pH 7.5 Tris buffer, and those for **5** were made in the former. For **3** (1.4×10^{-3} M) in 0.10 M NaBr two populations were observed with hydrodynamic diameters of 5 ± 1 nm (82 ± 3 vol %) and 24 ± 2 nm (17 ± 3 vol %). The size of the first is consistent with spherical micelles.[12] The second population is large enough to correspond to small unilamellar vesicles, but taken together the two populations most likely represent the extremes of an asymmetric particle size distribution including spherical and rod-shaped micelles.[13] For **3** (1.2(1.8) x 10^{-3} M) in the buffer a single population was observed with a diameter of 4.0 ± 0.4 nm. For **5** (1.2×10^{-3} M) a single population was observed with a diameter of 6.9 ± 0.3 nm. Thus both **3** and **5**, which differ in the positions of their linking groups, form micelles. Other double-chain, double-cationic head group surfactants have also been reported to form micelles,[3] as do most double-chain, double-anionic head group surfactants. In contrast, Ringsdorf and co-workers[4c] have reported vesicle formation by two surfactants of the latter type.

The cmc's at 25 °C of **3** in H_2O and 0.10 M NaBr are 6.8 and 1.5×10^{-4} M, respectively, and that of **5** in the latter is 3.3×10^{-4} M. The cmc's in H_2O at 25 °C of **7** and **8** are 2.1 and 1.9×10^{-3} M, respectively, and that of **9** is 6.5×10^{-4} M. Also, the Krafft temperatures of surfactants **3**, **5**, and **7-9** in H_2O are uniformly <25 °C. The cmc of **19**, the parent single-chain surfactant, is 1.5×10^{-4} M in H_2O at 25 °C.[14] Thus the cmc's of double-chain surfactants **3** and **5** and functionalized surfactants **7–9** are uniformly greater than that of **19**.

$C_{18}H_{37}N^+Me_3\ Br^-$

19

The hydrolyses of surfactants **3** to **7** and **8** (eq 1) and of **5** to **7** and **9** (eq 2) in 5.5 M HBr at 40 °C were ≥95% and ≥90% complete within 600 and 360 min, respectively. Controls demonstrated that **7-9** are stable under the reaction conditions for ≥24 h. The modest hydrolytic reactivities of **3** and **5** are characteristic of cationic ketal-based cleavable surfactants.[13,15] Surfactants **3** and **5** are in fact somewhat less reactive than related second generation single-chain cleavable surfactants.[13]

Both single-chain daughter surfactants **7** and **8** have cmc's greater than that of **3**. Since it is possible to convert micellar **3** into nonaggregated **7** and **8** (by operating at a concentration of **3** below the cmc's of **7** and **8**), micellar **3** could be used as a storage and release device. A water-insoluble compound could be solubilized in micellar **3** and then desolubilized as desired by hydrolysis of **3**. This process would not be complicated by the formation of a water-insoluble compound derived from **3**, as would be the case with first generation cleavable surfactants.

As noted above, **3** and **5** were each obtained as a 1:1 mixture of diastereomers in their syntheses from the respective single-chain surfactants in Schemes 1 and 4. The single-chain surfactants likely form mixed reversed micelles in CH_2Cl_2.[16] There are two limiting orientations of the average plane of the dioxolane ring of **3**(**5**) with respect to the radial axis of a reversed micelle: parallel and perpendicular. If **7** and **8**(**9**) are in extended conformations within a reversed micelle and the ratio of diastereomeric products **3a**(**5a**) and **3b**(**5b**) is kinetically controlled, the ring closure step most reasonably produces the dioxolane ring parallel to the reversed micelle axis. In establishing this orientation for both **3a**(**5a**) and **3b**(**5b**), the head groups and alkyl chains of reactants **7** and **8**(**9**) can reside in their preferred microenvironments, *i.e.*, the former in the reversed micelle core and the latter radiating outward to the CH_2Cl_2 bulk phase. With the head groups and alkyl chains of **7** and **8**(**9**) in their preferred microenvironments, **3a**(**5a**), but not **3b**(**5b**), can be formed with a perpendicular dioxolane ring. The formation of **3b**(**5b**) with a perpendicular dioxolane ring would require misalignment of either **7** or **8**(**9**), with its head group and alkyl chain directed toward unfavorable microenvironments, the CH_2Cl_2 bulk phase and the micelle core, respectively. Porter and co-workers found interfacial control of stereochemistry in the base-catalyzed equilibration of ketone-linked, double-chain, double-anionic head group surfactants in aqueous aggregates.[4b]

In summary, we have prepared and characterized cleavable double-chain, double-cationic head group surfactants **3** and **5**. They form micelles and by acid-catalyzed hydrolysis can be cleaved into single-chain surfactants. Micellar **3** has potential as a storage and release device.

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Experimental Section

General Procedures and Materials. ^1H (270 and 400 MHz) and ^{13}C (67.9 and 100.6 MHz) NMR spectra were recorded in $CDCl_3$ with Me_4Si and $CDCl_3$ (center line at 77.00 ppm relative to Me_4Si) as internal standards, respectively. J values are in hertz. High resolution mass spectra were obtained at the Midwest Center for Mass Spectrometry with partial support by the National Science Foundation, Biology Division (Grant No. DIR9017262). Krafft temperatures were determined according to a literature procedure.[17] The cmc measurements, flash chromatography, and preparative TLC were performed as before.[18] The pH 7.5 Tris buffer used for DLLS was prepared as previously described.[18a] $CHCl_3$ and $CDCl_3$ were stored over anhydrous Na_2CO_3. THF and C_6H_6 were distilled from $LiAlH_4$, and anhydrous Et_2O from benzophenone sodium ketyl. Extracts were dried over $MgSO_4$ or Na_2SO_4. All melting points were taken with open capillary tubes and are uncorrected. Unless noted otherwise, the ratios describing the compositions of solvent mixtures represent relative volumes. Elemental analyses were performed by Atlantic Microlab, Atlanta, GA.

((*Z*)-9-Octadecenyl)trimethylammonium Bromide (12).[8] In standard fashion, methyl (*Z*)-9-octadecenoate (Aldrich) was reduced with $LiAlH_4$ in anhydrous Et_2O to give (90%) (*Z*)-9-octadecen-1-ol[19] as an oil. By a literature procedure,[20] 0.82 g (3.1 mmol) of this alcohol gave crude bromo alkene that was chromatographed on a 10- × 2.5-cm column of silica gel packed in hexane. Elution with 5:1 hexane-ether yielded 0.94 g (92%) of (*Z*)-1-bromo-9-octadecene[21] as an oil. A solution of 0.90 g (2.7 mmol) of this bromo alkene in 30 mL of 25% (w/v) Me_3N-MeOH was stirred at 25 °C for 3 d and then refluxed for 2 h and rotary evaporated. The resultant solid was chromatographed on a 10- x 2.5-cm column of neutral aluminum oxide (J. T. Baker 0537) packed in, and eluted with, 1:4 MeOH–$CHCl_3$ to give 0.59 g (56%) of **12** as a solid: mp 223–228 °C (lit.[8] mp 225–230 °C). Anal. Calcd for $C_{21}H_{44}BrN{\cdot}0.25H_2O$: C, 63.86; H, 11.36. Found: C, 63.81; H, 11.31.

(*threo*-9,10-Dihydroxyoctadecyl)trimethylammonium Bromide (7). A modified literature procedure[22] was used. A mixture of 68 mg (0.17 mmol) of **12**, 3.0 mL of 88% formic acid, and 3.0 mL (50 mmol) of 30% H_2O_2 was stirred at 40 °C under N_2 for 24 h and then rotary evaporated to near, but not complete, dryness. A solution of the residue in 25 mL of 3.0 M KOH was held at 80 °C for 3 h, cooled to 25 °C, acidified to pH 1 with concentrated hydrobromic acid, and lyophilized. The residue was slurry-extracted with two 100-mL portions of $CHCl_3$, and the combined extracts were dried and rotary evaporated to give an oil. This material was chromatographed on a 10- × 1-cm column of neutral aluminum oxide packed in $CHCl_3$ with 1:4 MeOH–$CHCl_3$ elution to give 22 mg (30%) of **7**: ^1H NMR (270 MHz) δ 3.63 (m, 2 H), 3.38–3.52 (m + s at 3.45, 11 H), 2.70 (br s, 2 H), 1.79 (m, 2 H), 1.20–1.58 (m, 26 H), 0.88 (t, 3 H); ^{13}C NMR (67.9 MHz) δ 74.48, 74.29, 66.89, 53.43, 33.68, 33.46, 31.85, 29.74, 29.59, 29.27, 28.96, 28.69, 28.42, 25.78, 25.28, 22.87, 22.64, 14.09. Anal. Calcd for $C_{21}H_{46}BrNO_2$: C, 59.42; H, 10.92. Found: C, 59.31; H, 10.87.

Ethyl 8-Oxooctadecanoate (13).[9] A literature procedure[9] was used to prepare (55%) 7-(ethoxycarbonyl)heptanoic acid[23] as an oil from octanedioic acid (Aldrich). By standard procedures this material gave (92%) 7–(ethoxycarbonyl)heptanoyl chloride[24] as an oil on reaction with $SOCl_2$. By the literature procedure,[9] 2.00 g (9.06 mmol) of this acid chloride ester was converted into 1.19 g (40%) of **13**: mp 37–38 °C (lit.[9] mp 37 °C).

Ethyl 7-(2-Decyl-1,3-dioxolan-2-yl)heptanoate (14). A solution of 3.2 g (9.8 mmol) of **13**, 0.70 g (11 mmol) of $HOCH_2$-CH_2OH, and 0.10 g of p-$MeC_6H_4SO_3H{\cdot}H_2O$ in 30 mL of C_6H_6 was refluxed under a Dean-Stark trap and N_2 for 6 h. After the addition of 100 mL of C_6H_6, the reaction mixture was washed with 10 mL of 1.0 M $NaHCO_3$, dried, and rotary evaporated to yield 3.0 g (83%) of **14** as an oil that was used without further purification: ^1H NMR (400 MHz) δ 4.12 (q, J = 7.1, 2 H), 3.92 (s, 4 H), 2.28 (t, J = 7.3, 2 H), 1.52–1.68 (m, 6 H), 1.20–1.30 (m, 25 H), 0.88 (t, 3 H); ^{13}C NMR (100.6 MHz) δ 173.81, 111.79, 64.86, 60.12, 37.13, 37.02, 34.32, 31.88, 29.92, 29.58, 29.29, 29.09, 24.89, 23.83, 23.64, 22.65, 14.21, 14.08. A portion of the above oil was chromatographed three times on 10- × 2.5-cm columns of neutral aluminum oxide packed in hexane with 9:1 hexane-ether as eluant to give an analytical sample. Anal. Calcd for $C_{22}H_{42}O_4$: C, 71.31; H, 11.42. Found: C, 71.37; H, 11.38.

7-(2-Decyl-1,3-dioxolan-2-yl)heptan-1-ol. By standard procedures, 2.9 g (7.8 mmol) of **14** was reduced with $LiAlH_4$ in anhydrous Et_2O to give crude product. Flash chromatography of this material on a 20- × 5-cm column of silica gel packed in hexane with 10:5:1 hexane-EtOAc-MeOH as eluant gave 2.3 g (90%) of the title compound as an oil: ^1H NMR (400 MHz) δ 3.92 (s, 4 H), 3.63 (t, J = 6.6, 2 H), 1.52–1.65 (m, 6 H), 1.20–1.41 (m, 25 H), 0.88 (t, 3 H); ^{13}C NMR (100.6 MHz) δ 111.87, 64.87, 63.05, 37.13, 37.09, 32.77, 31.90, 29.94, 29.87, 29.61, 29.37, 29.32, 25.65, 23.86, 23.76, 22.68, 14.11. Anal. Calcd for $C_{20}H_{40}O_3$: C, 73.12; H, 12.27. Found: C, 72.97; H, 12.25.

2-Decyl-2-(7-bromoheptyl)-1,3-dioxolane (15). A literature procedure[25] was used to convert 50 mg (0.15 mmol) of the above ketal alcohol into 53 mg of a 9:1 mixture (^1H NMR analysis) of 7-(2-decyl-1,3-dioxolan-2-yl)heptyl methanesulfonate and 8-oxooctadecyl methanesulfonate that was used without further purification. A solution of this methanesulfonate mixture and 18 mg (0.21 mmol) of anhydrous LiBr in 5 mL of THF was refluxed for 12 h under N_2 and rotary evaporated. The residue was extracted with two 25-mL portions of CH_2Cl_2, and the combined extracts were washed with 20 mL each of H_2O and saturated aqueous NaCl and then dried and rotary evaporated. Preparative TLC of the resultant oil on silica gel with 6:1 hexane-ether as eluant gave two bands. The band with R_f = 0.58 afforded 33 mg (56%) of **15** as an oil: ^1H NMR (270 MHz) δ 3.92 (s, 4 H), 3.40 (t, J = 6.9, 2 H), 1.85 (p, J = 7.3, 2 H), 1.52–1.66 (m, 4 H), 1.18–1.48 (m, 26 H), 0.88 (t, 3 H); ^{13}C NMR (67.9 MHz) δ 111.68, 64.76, 37.04, 36.95, 33.75, 32.71, 31.83, 29.85, 29.60, 29.53, 29.24, 28.63, 28.00, 23.76, 23.61, 22.59, 14.04. The band with R_f = 0.55 yielded a solid that was recrystallized from MeOH (4 °C) to give 17 mg (32%) of **11**: mp 32–33 °C. The mp and ^1H NMR spectrum of this material were identical to those given below for **11**.

1-Bromo-8-octadecanone (11). A solution of 59 mg (0.15 mmol) of **15**, 1 mL of 1.0 M HCl, and 10 mL of Me_2CO was stirred at 25 °C for 2 h. The Me_2CO was rotary evaporated and the residue extracted with 100 mL of Et_2O. The extract was dried and rotary evaporated to leave a solid that was recrystallized from MeOH (4 °C) to yield 38 mg (73%) of **11**: mp 32–33 °C; ^1H NMR (270 MHz) δ 3.40 (t, J = 6.6, 2 H), 2.38 (t, J = 7.3, 2 H), 2.39 (t, J = 7.3, 2 H), 1.85 (p, J = 7.3, 2 H), 1.58 (m, 4 H), 1.20–1.50 (m, 20 H), 0.88 (t, 3 H); ^{13}C NMR (67.9 MHz) δ 211.42, 42.82, 42.60, 33.84, 32.69, 31.84, 29.52, 29.43, 29.38, 29.25, 29.00, 28.52, 27.94, 23.86, 23.65, 22.64, 14.07. Anal. Calcd for $C_{18}H_{35}BrO$: C, 62.24; H, 10.16. Found C: 62.29; H, 10.19.

(8-Oxooctadecyl)trimethylammonium Bromide (8). By the procedure used for **12**, 50 mg (0.14 mmol) of **11** was converted into crude **8** as a solid. Recrystallization of this material from Me_2CO (4 °C) gave 47 mg (83%) of **8**: mp 110–112 °C; ^1H NMR (270 MHz) δ 3.61 (m, 2 H), 3.48 (s, 9 H), 2.32–2.48 (m, 4 H), 1.78 (m, 2 H), 1.54 (m, 4 H), 1.20–1.48 (m, 20 H), 0.88 (t, 3 H); ^{13}C NMR (67.9 MHz) δ 211.44, 66.79, 53.33, 42.85, 42.41, 31.81, 29.49, 29.42, 29.35, 29.22, 28.81, 28.70, 25.80, 23.83, 23.34, 22.94, 22.60, 14.04. Anal. Calcd for $C_{21}H_{44}BrNO$: C, 62.05; H, 10.91. Found: C, 62.03; H, 10.76.

***threo*-9,10-Dihydroxyoctadecanoic Acid (16).**[10] By a literature procedure[22] methyl (*Z*)-9-octadecenoate was converted (91%) into **16**: mp 89–90 °C (lit.[10] mp 95 °C).

***trans*-8-(2,2-Dimethyl-5-octyl-1,3-dioxolan-4-yl)-octanoic Acid.**[26] A mixture of 9.9 g (31 mmol) of **16**, 1.0 mL of concentrated sulfuric acid, 750 mL of Me_2CO, and 0.7 g of 4 Å

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molecular sieves was stirred at 25 °C for 24 h. Then 13 g (0.12 mmol) of Na_2CO_3 was added, and the mixture was stirred for an additional 24 h and filtered through a 6.5- × 3.5-cm column of silica gel. Rotary evaporation of the filtrate yielded 9.3 g (84%) of the title compound as an oil.

***trans*-8-(2,2-Dimethyl-5-octyl-1,3-dioxolan-4-yl)octan-1-ol (17).**[13] By standard procedures, 9.6 g (27 mmol) of the above ketal acid was reduced with $LiAlH_4$ in anhydrous Et_2O to give 7.1 g (76%) of **17** as an oil.

***trans*-2,2-Dimethyl-4-(8-bromooctyl)-5-octyl-1,3-dioxolane.** By a literature procedure,[20] 0.20 g (0.58 mmol) of **17** gave crude bromo ketal that was chromatographed on a 5- × 2.5-cm column of silica gel packed in hexane with 5:1 hexane-ether as eluant to give 0.20 g (85%) of the title compound as an oil: ^{1}H NMR (270 MHz) δ 3.59 (m, 2 H), 3.41 (t, J = 6.9, 2 H), 1.85 (p, J = 7.3, 2 H), 1.21–1.58 (m + s at 1.38, 32 H), 0.88 (t, 3 H); ^{13}C NMR (67.9 MHz) δ 107.70, 81.01, 34.02, 33.02, 33.78, 31.86, 29.79, 29.64, 29.48, 29.28, 29.26, 28.67, 28.12, 27.32, 26.16, 26.13, 22.65, 14.10. Anal. Calcd for $C_{21}H_{41}BrO_2$: C, 62.21; H, 10.19. Found: C, 61.97; H, 10.07.

***threo*-1-Bromo-9,10-octadecanediol (10).** A solution of 0.18 g (0.44 mmol) of the above bromo ketal, 1.0 mL of 2.0 M HBr, and 5 mL of EtOH was refluxed for 12 h and rotary evaporated to remove EtOH. The residue was extracted with 100 mL of hexane, which was dried and rotary evaporated to give a solid. Recrystallization of this material from hexane (25 °C) afforded 0.14 g (87%) of **10**: mp 53–54 °C; ^{1}H NMR (270 MHz) δ 3.35–3.52 (m, 4 H), 2.23 (br s, 2 H), 1.86 (p, J = 7.3, 2 H), 1.18–1.62 (m, 26 H), 0.88 (t, 3 H); ^{13}C NMR (67.9 MHz) δ 74.48, 74.45, 33.98, 33.57, 33.53, 32.74, 31.83, 29.65, 29.51, 29.33, 29.24, 28.66, 28.09, 25.63, 25.59, 22.62, 14.07. Anal. Calcd for $C_{18}H_{37}BrO_2$: C, 59.17; H, 10.21. Found: C, 59.18; H, 10.16.

***r*-2-(7-Bromoheptyl)-2-decyl-*c*-4-(8-bromooctyl)-*t*-5-octyl-1,3-dioxolane (4a) and *r*-2-(7-Bromoheptyl)-2-decyl-*t*-4-(8-bromooctyl)-*c*-5-octyl-1,3-dioxolane (4b).** A solution of 35 mg (0.10 mmol) of **10**, 40 mg (0.12 mmol) of **11**, and 8 mg of PPTS in 5 mL of C_6H_5Me was refluxed under a Dean-Stark trap and N_2 for 30 h and rotary evaporated to leave an oil. Preparative TLC of this material on silica gel with 10:1 hexane-Et_2O elution afforded 51 mg (73%) of **4** (R_f = 0.9) as an oil: ^{1}H NMR (270 MHz) δ 3.54 (br s, 2 H), 3.40 (t, J = 6.9, 4 H), 1.88 (p, J = 7.3, 4 H), 1.20–1.62 (m, 54 H), 0.88 (t, 6 H); ^{13}C NMR (67.9 MHz) δ 110.93, 81.22, 81.16, 38.56, 38.45, 33.95, 32.95, 32.80, 31.92, 31.87, 29.94, 29.80, 29.63, 29.48, 29.35, 29.29, 29.26, 28.73, 28.69, 28.13, 26.16, 23.79, 23.64, 22.68, 14.11. Anal. Calcd for $C_{36}H_{70}Br_2O_2$: C, 62.24; H, 10.16. Found: C, 62.17; H, 10.13.

Diastereomers **4a** and **4b** were inseparable by HPLC on a 25-cm × 4.6-mm (i.d.) 10-μm C18 column (Alltech 60086) with a 3-cm × 4.6-mm (i.d.) 10-μm C18 guard column (Brownlee 18-GU) and UV detection (215 nm). With 1:49 THF-MeOH as eluant and flow rate = 2.0 mL/min, a single peak with retention time = 32.6 min was obtained for the above mixture of **4a** and **4b**. TLC analysis on silica gel or aluminum oxide with hexane as eluant gave only one spot (R_f = 0.8 on each). Since a 1:1 mixture of **3a** and **3b** was obtained below from the above mixture of **4a** and **4b**, it is assumed that the ratio of the latter compounds was also 1:1.

***r*-2-(7-(Trimethylammonio)heptyl)-2-decyl-*c*-4-(8-(trimethylammonio)octyl)-*t*-5-octyl-1,3-dioxolane Dibromide (3a) and *r*-2-(7-(Trimethylammonio)heptyl)-2-decyl-*t*-4-(8-(trimethylammonio)octyl)-*c*-5-octyl-1,3-dioxolane Dibromide (3b) from Dibromo Ketals 4.** By the procedure used for **12**, 0.12 g (0.17 mmol) of the above **4** gave 0.13 g (94%) of **3** as a solid. This material was purified by column chromatography on basic aluminum oxide (J. T. Baker 0539) packed in 5% EtOH in 1:1 MeCN-$CHCl_3$ and eluted with 100 mL each of 5% and 6%, 200 mL of 7%, and 100 mL of 20% EtOH in 1:1 MeCN-$CHCl_3$. Surfactant **3** eluted with the latter two eluants: ^{1}H NMR (270 MHz) δ 3.42–3.76 (m + s at 3.48, 24 H), 1.78 (m, 4 H), 1.19–1.64 (m + s at 1.26, 54 H), 0.88 (t, 6 H); ^{13}C NMR (67.9 MHz) δ 110.94, 110.72, 81.31, 81.17, 81.02, 66.78, 66.65, 53.34, 38.71, 38.35, 33.15, 32.89, 32.66, 31.85, 31.82, 29.90, 29.77, 29.73, 29.58, 29.43, 29.29, 29.21, 29.01, 28.93, 26.14, 25.88, 23.73, 23.53, 23.22, 23.16, 22.61, 14.04. Anal. Calcd for $C_{42}H_{88}Br_2N_2O_2 \cdot 1.5H_2O$: C, 60.05; H, 10.92. Found: C, 59.89; H, 10.81.

HPLC analysis was performed on a 25-cm × 4.6-mm (i.d.) 8-μm C18 column with a 1.5-cm × 4.6-mm (i.d.) 8-μm C18 guard column (Rainin 83–201-C and 83–201-G, respectively) and RI detection. With 1:49 aqueous 0.20 M $NaClO_4$-MeOH as eluant and flow rate = 1.5 mL/min, two peaks in a 1:1 ratio with retention times = 5.5 and 6.0 min were obtained for the above mixture of **3a** and **3b**.

Surfactant 3 from Surfactants 7 and 8. A mixture of 80 mg (0.19 mmol) of **7**, 20 mg (0.049 mmol) of **8**, 5 mg of *p*-$MeC_6H_4SO_3H \cdot H_2O$, 100 mg of 4 Å molecular sieves, and 5.0 mL of CH_2Cl_2 was stirred under N_2 for 7 d, filtered, and rotary evaporated to leave crude product that was purified as above to give 30 mg (75%) of **3**. By the HPLC conditions used for the analysis of **3** prepared from **4**, the **3a/3b** ratio = 1.0.

Methyl 4-Oxooctadecanoate.[11] By standard procedures *mono*-methyl succinate (Aldrich) gave (88%) 3-(methoxycarbonyl)propanoyl chloride[27] as an oil on reaction with $SOCl_2$. By a literature procedure,[9] 5.0 g (33 mmol) of this acid chloride ester was converted into 2.2 g (21%) of the title compound: mp 47–48 °C (lit.[11] mp 47.9–48.0 °C).

Methyl 3-(2-Tetradecyl-1,3-dioxolan-2-yl)propanoate. By the procedure used for **14**, 2.0 g (6.4 mmol) of the above keto ester was converted into 2.0 g (88%) of the title compound as an oil, which was used without further purification: ^{1}H NMR (270 MHz) δ 3.93 (s, 4 H), 3.67 (s, 3 H), 2.37 (t, J = 7.6, 2 H), 1.99 (m, J = 7.9, 2 H), 1.58 (m, 2 H), 1.25 (s, 24 H), 0.88 (t, 3 H); ^{13}C NMR (67.9 MHz) δ 174.10, 110.87, 65.01, 51.54, 37.41, 31.99, 31.90, 29.87, 29.63, 29.56, 29.35, 28.68, 23.79, 22.66, 14.09. An analytical sample was obtained by column chromatography on a 5- × 0.25-cm column of neutral aluminum oxide packed in hexane with 10:5:1 hexane-EtOAc-MeOH as eluant. Anal. Calcd for $C_{21}H_{40}O_4$: C, 70.74; H, 11.31. Found: C, 70.67; H, 11.29.

3-(2-Tetradecyl-1,3-dioxolan-2-yl)propan-1-ol. By standard procedures, 1.9 g (5.3 mmol) of the above ketal ester was reduced with $LiAlH_4$ in anhydrous Et_2O to give crude product. Column chromatography of this material on a 10- × 2.5-cm column of neutral aluminum oxide packed in hexane with 1:1 hexane-EtOAc as eluant gave 1.5 g (87%) of the title compound as an oil: ^{1}H NMR (270 MHz) δ 3.95 (s, 4 H), 3.64 (t, J = 5.9, 2 H), 2.17 (br s, 1 H), 1.58–1.79 (m, 6 H), 1.25 (s, 24 H), 0.88 (t, 3 H); ^{13}C NMR (67.9 MHz) δ 111.70, 64.83, 63.06, 37.04, 33.62, 31.88, 29.88, 29.63, 29.56, 29.33, 26.96, 23.85, 22.64, 14.07. Anal. Calcd for $C_{20}H_{40}O_3$: C, 73.12; H, 12.27. Found: C, 73.05; H, 12.23.

1-Bromo-4-octadecanone (18). By a literature procedure,[25] 0.50 g (1.5 mmol) of the above ketal alcohol was converted into 3-(2-tetradecyl-1,3-dioxolan-2-yl)propyl methanesulfonate, which was used immediately without further purification. By the procedure used for the preparation of **15**, the methanesulfonate ketal gave crude 2-tetradecyl-2-(3-bromopropyl)-1,3-dioxolane as an oil. A solution of this material in 2.0 mL of 2 M HBr and 50 mL of Me_2CO was stirred at 25 °C for 24 h. The Me_2CO was removed by rotary evaporation and the residue extracted with 200 mL of Et_2O. The extract was dried and rotary evaporated, and the resultant solid was recrystallized from MeOH (4 °C) to give 0.37 g (71%) of **18**: mp 34–35 °C; ^{1}H NMR (270 MHz) δ 3.45 (t, J = 6.6, 2 H), 2.61 (t, J = 6.9, 2 H), 2.41 (t, J = 7.3, 2 H), 2.12 (p, J = 6.6, 2 H), 1.58 (m, 2 H), 1.25 (s, 22 H), 0.88 (t, 3 H); ^{13}C NMR (67.9 MHz) δ 209.85, 43.02, 40.40, 33.41, 31.88, 29.62, 29.44, 29.36, 29.33, 29.18, 26.36, 23.85, 22.66, 14.07. EI HRMS calcd for $C_{18}H_{35}{}^{79}BrO$: 346.1872, found 346.1875.

(4-Oxooctadecyl)trimethylammonium Bromide (9). By the procedure used for **12**, 0.50 g (1.4 mmol) of **18** gave crude **9** as a solid. This material was recrystallized twice from Me_2CO (5 °C) to yield 0.41 g (71%) of **9** as a solid: mp 148–150 °C; ^{1}H NMR (400 MHz) δ 3.72 (m, 2 H), 3.45 (s, 9 H), 2.65 (t, J = 6.2, 2 H), 2.42 (t, J = 7.5, 2 H), 2.03 (m, 2 H), 1.54 (m, 2 H), 1.25 (s, 22 H), 0.88 (t, 3 H); ^{13}C NMR (67.9 MHz) δ 209.34, 65.66, 53.37, 42.79, 37.92, 31.87, 29.60, 29.41, 29.34, 29.30, 29.13, 23.68, 22.63, 17.02, 14.07. Anal. Calcd for $C_{21}H_{44}BrNO$: C, 62.05; H, 10.91. Found: C, 61.92; H, 10.93.

***r*-2-(3-Bromopropyl)-2-tetradecyl-*c*-4-(8-bromooctyl)-*t*-5-octyl-1,3-dioxolane (6a) and *r*-2-(3-Bromopropyl)-2-tetradecyl-*t*-4-(8-bromooctyl)-*c*-5-octyl-1,3-dioxolane (6b).** A solution of 0.20 g (0.55 mmol) of **10**, 0.20 g (0.58 mmol) of **18**, and 20 mg of PPTS in 15 mL of C_6H_5Me was refluxed under a Dean-Stark trap and N_2 for 24 h and rotary evaporated to leave

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an oil. This material was chromatographed on a 10- × 2.5-cm column of neutral aluminum oxide packed in, and eluted with, hexane to give 0.30 g (78%) of **6** as a solid: ^{1}H NMR (400 MHz) δ 3.55 (m, 2 H), 3.39–3.48 (m, 4 H), 1.94 (m, 2 H), 1.86 (m, 2 H), 1.72 (t, J = 7.9, 2 H), 1.58 (m, 2 H), 1.21–1.52 (m + s at 1.26, 50 H), 0.88 (m, 6 H); ^{13}C NMR (100.6 MHz) δ 110.36, 81.49, 81.26, 38.70, 36.83, 34.32, 34.00, 32.99, 32.97, 32.85, 32.78, 31.92, 31.86, 29.87, 29.70, 26.61, 29.46, 29.36, 29.26, 28.67, 28.12, 27.46, 26.18, 23.76, 22.66, 14.12. Anal. Calcd for $C_{36}H_{70}Br_2O_2$: C, 62.24; H, 10.16. Found: C, 61.97; H, 10.04.

Diastereomers **6a** and **6b** were inseparable by HPLC with the same columns, eluant, and detection used for dibromo ketals **4**. Analysis of the above mixture of **6a** and **6b** gave a single peak with retention time = 39.2 min using flow rate = 1.5 mL/min. Since a 1:1 mixture of **5a** and **5b** was obtained below from this mixture of **6a** and **6b**, it is assumed that the ratio of the latter compounds was also 1:1.

***r*-2-(3-(Trimethylammonio)propyl)-2-tetradecyl-*c*-4-(8-(trimethylammonio)octyl)-*t*-5-octyl-1,3-dioxolane Dibromide (5a) and *r*-2-(3-(Trimethylammonio)propyl)-2-tetradecyl-*t*-4-(8-(trimethylammonio)octyl)-*c*-5-octyl-1,3-dioxolane Dibromide (5b).** By the procedure used for **12**, 0.20 g (0.29 mmol) of the above **6** gave crude product, which was column chromatographed on a 10- × 2.5-cm column of neutral aluminum oxide packed in CH_2Cl_2 and eluted with 10:1 CH_2Cl_2-MeOH to give 0.20 g (85%) of **5** as a solid. This material was purified further by column chromatography on basic aluminum oxide packed in, and eluted with, 10% EtOH in MeCN-$CHCl_3$: ^{1}H NMR (270 MHz) δ 3.41–3.78 (m + 2 s at 3.46 and 3.48, 24 H), 1.20–1.88 (m + s at 1.26, 58 H), 0.88 (m, 6 H); ^{13}C NMR (100.6 MHz) δ 109.85, 109.62, 81.40, 66.89, 66.57, 66.50, 53.29, 38.71, 34.12, 33.35, 32.56, 32.53, 32.43, 31.82, 31.76, 29.74, 29.60, 29.42, 29.37, 29.32, 29.26, 29.16, 28.98, 28.75, 26.25, 26.22, 26.06, 25.95, 25.68, 23.76, 23.06, 23.03, 22.57, 17.50, 17.46, 14.02. Anal. Calcd for $C_{42}H_{88}Br_2N_2O_2 \cdot 0.5H_2O$: C, 61.37; H, 10.91. Found: C, 61.35; H, 10.89. FAB HRMS (3-nitrobenzyl alcohol matrix) calcd for $C_{42}H_{88}{}^{79}BrN_2O_2$ (dication·Br^-) 731.6029, found 731.6040.

With the HPLC conditions used for the analysis of **3**, two peaks in a 1:1 ratio with retention times = 7.8 and 8.8 min were obtained for the above mixture of **5a** and **5b**.

Surfactant 5 from Surfactants 7 and 9. A mixture of 20 mg (0.047 mmol) of **7**, 20 mg (0.049 mmol) of **9**, 5 mg of p-$MeC_6H_4SO_3H \cdot H_2O$, 100 mg of 4 Å molecular sieves, and 5.0 mL of CH_2Cl_2 was stirred under N_2 for 7 d, filtered, and rotary evaporated to leave material that was purified as above to give 33 mg (86%) of **5**. The mixture of **5a** and **5b** was analyzed by HPLC with the same columns, eluant, and detection used for the analysis of **3**. With flow rate = 1.0 mL/min, two peaks in a 1:1 ratio with retention times = 11.4 and 12.3 min were obtained.

DLLS. Measurements were made at 23 °C on the instrumentation described previously.[9] A solution of 1–3 mg of surfactant in 2 mL of $CHCl_3$ (HPLC-grade stored over Na_2CO_3) was rotary evaporated and the resultant thin film dried for 12 h (25 °C, 0.1 mmHg). Then an aliquot of 0.10 M NaBr or the pH 7.5 Tris buffer was added, and the solution at 55 °C was sonicated for 30 min or vortexed for 4 min.[18a] Then it was held at 55 °C for 30 min and at 25 °C for 30 min, followed by filtration and performance of the DLLS run using the procedure described previously[13] with the substitution of *cis* and *trans*-decalin for dodecane (index matching).

Hydrolysis of 3 and 5. A 1.3 × 10^{-3} M solution of **3** in 5.5 M HBr was held at 40 °C. At various times a 3-mL aliquot was removed, adjusted to pH 8–9 with 4.4 M NaOH, and lyophilized. The residue was extracted with CH_2Cl_2, and the extract was filtered and rotary evaporated. The extent of hydrolysis of **3** to **7** and **8** was determined by ^{1}H NMR analysis (270 MHz) of the residue. The signal for CH_2COCH_2 of **8** at δ 2.32–2.48 was compared to that for CH_3CH_2 of **3**, **7**, and **8** at δ 0.88. The extents of hydrolysis were 42%, 56%, and ≥95% at 180, 360, and 600 min, respectively.

The procedure for the hydrolysis of **5** to **7** and **9** was identical to that for **3**. The signals for CH_2COCH_2 of **9** at δ 2.42 and 2.65 were compared to that for CH_3CH_2 of **5**, **7**, and **9** at δ 0.88. The extents of hydrolysis were 59% and ≥90% at 150 and 360 min, respectively.

A 1.3 × 10^{-3} M solution of **7** in 5.5 M HBr was held at 40 °C for 24 h and then worked up as above. By ^{1}H NMR analysis (270 MHz) the resultant residue contained only **7**. Analogous controls with **8** and **9** indicated that they are also stable to the hydrolysis reactions conditions.

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Supplementary Material Available: ^{1}H and ^{13}C NMR spectra of **15** and **18**; ^{1}H NMR data with peak assignments (7 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.