

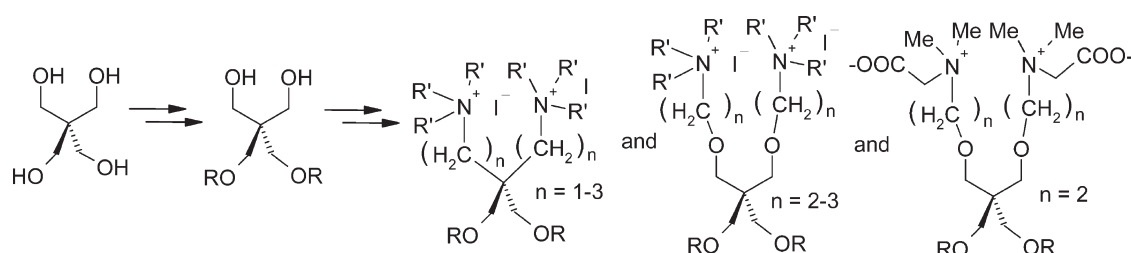
Synthesis of Surfactants Based on Pentaerythritol. I. Cationic and Zwitterionic Gemini Surfactants

Nusrat Jahan,[†] Nawal Paul,[†] Christian J. Petropolis,^{†,‡} D. Gerrard Marangoni,^{*,‡} and T. Bruce Grindley^{*,†}

[†]Department of Chemistry, Dalhousie University, Halifax, NS, Canada B3H 4J3, and [‡]Department of Chemistry, St. Francis Xavier University, Antigonish, NS, Canada B2G 2W5

bruce.grindley@dal.ca; gmarango@stfx.ca

Received July 14, 2009



Simple strategies for the synthesis of five series of cationic gemini surfactants and one series of zwitterionic gemini surfactants from pentaerythritol have been developed. Two lipophilic groups were introduced onto pentaerythritol by alkylation of the known compound, *O*-benzylidenepentaerythritol, with 1-bromooctane, 1-bromodecane, 1-bromododecane, and 1-bromotetradecane. Hydrogenolysis of the benzylidene acetals gave diols which were converted into three different series of trimethylammonium derivatives. The diiodides derived from the diols could be displaced by dimethylamine, even though they are adjacent to a quaternary carbon atom. Alkylation with methyl iodide gave the first series. The iodides were easily displaced by cyanide ion and the resulting dinitriles were hydrolyzed, converted to *N,N*-dimethylamides, and reduced to give a second series. Oxidation of the diols to dialdehydes under Swern conditions followed by Horner–Wadsworth–Emmons reactions with diethyl *N,N*-dimethylcarbamoylmethylphosphonate followed by two-stage reduction gave a third series. The dialkoxides derived from the four di-*O*-alkylpentaerythritol diols were reacted with 2-dimethylaminoethyl chloride and 3-dimethylaminopropyl chloride in neighboring-group assisted double Williamson ether syntheses to give precursors to two more series. As expected because the neighboring group participation occurs through a four-membered-ring intermediate, considerably more vigorous conditions were required for the reactions with 3-dimethylaminopropyl chloride. 2-Diethylaminoethyl bromide was found to be less reactive than 2-dimethylaminoethyl chloride. The products were alkylated with methyl iodide and, in some cases, other alkyl halides to give cationic gemini surfactants. Alkylation of one series with ethyl bromoacetate followed by anion exchange resin catalyzed ester hydrolysis gave zwitterionic gemini surfactants. The members of all series have superior surfactant properties.

Introduction

Gemini surfactants have attracted considerable attention^{1–9} since the creation of the term by Menger.¹⁰ This term

is applied to compounds having two or more lipophilic units connected at or close to the polar head groups. Gemini surfactants display critical micellization concentrations that

*To whom correspondence should be addressed. Phone: 1-902-494-2041 (T.B.G.) and 1-902-867-2324 (D.G.M.).

(1) Menger, F. M.; Keiper, J. S. *Angew. Chem., Int. Ed.* **2000**, *39*, 1907–1920.

(2) Zana, R. *Adv. Colloid Interface Sci.* **2002**, *97*, 205–253.

(3) Rosen, M. J. *Cosmet. Toiletries* **1998**, *113*, 49–55.

(4) Wettig, S. D.; Verrall, R. E.; Foldvari, M. *Curr. Gene Ther.* **2008**, *8*, 9–23.

(5) Alami, E. O.; Holmberg, K. *Adv. Colloid Interface Sci.* **2003**, *100*, 13–46.

(6) Yao, Z. G.; Li, G. Z.; Dong, F. L.; Hu, A. X. *Prog. Chem.* **2004**, *16*, 349–364.

(7) Shukla, D.; Tyagi, V. K. *J. Oleo Sci.* **2006**, *55*, 215–226.

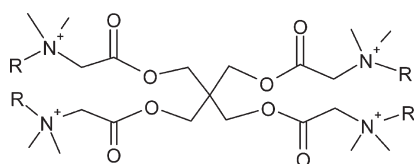
(8) Shukla, D.; Tyagi, V. K. *J. Oleo Sci.* **2006**, *55*, 381–390.

(9) Bombelli, C.; Giansanti, L.; Luciani, P.; Mancini, G. *Curr. Med. Chem.* **2009**, *16*, 171–183.

(10) Menger, F. M.; Littau, C. A. *J. Am. Chem. Soc.* **1991**, *113*, 1451–1452.

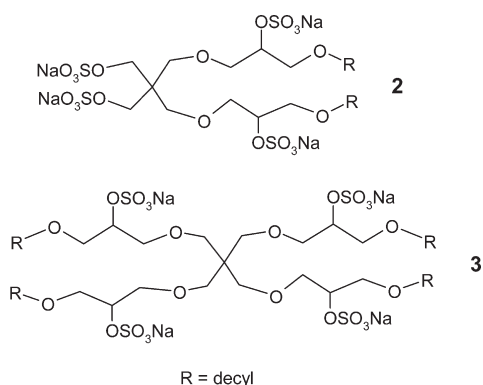
are 1 to 2 orders of magnitude lower than those of the corresponding conventional surfactants with only a single head group and also are much more efficient at lowering surface tensions of aqueous solutions. There has been considerable interest in exploring how structural variations influence surfactant properties, particularly in how head group spacing influences these properties.^{11–21}

Pentaerythritol is a convenient starting material for the preparation of gemini surfactants as will be shown herein. Two previous reports^{22,23} have described surfactants prepared from pentaerythritol. Those of type **1** had poor solubility in water.²²



1 R = hexyl, octyl, and dodecyl

Compounds **2** and **3** had quite low CMCs but only the two compounds shown and a disulfated derivative were prepared.²³ This publication will describe the synthesis of a comprehensive set of pentaerythritol-based cationic gemini surfactants designed to determine how the structure of the surfactant influences its properties.

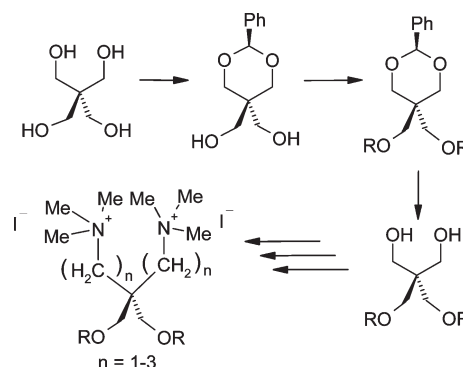


Results and Discussion

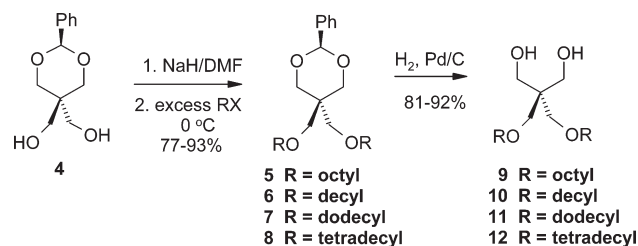
Cationic Gemini Surfactants Derived from Pentaerythritol with Branching Chains Only Containing Carbon Atoms. Synthetic Strategy. The synthetic strategy adopted for the

- (11) Zana, R.; Benraou, M.; Rueff, R. *Langmuir* **1991**, *7*, 1072–1075.
 (12) Bhattacharya, S.; Haldar, J. *Colloids Surf., A* **2002**, *205*, 119–126.
 (13) Zana, R. *J. Colloid Interface Sci.* **2002**, *248*, 203–220.
 (14) Ali, H. E. S. *Tenside, Surfactants, Deterg.* **2007**, *44*, 281–286.
 (15) Cao, X. L.; Li, Z. Q.; Song, X. W.; Cui, X. H.; Wei, Y. P.; Cheng, F.; Wang, J. *J. Surfactants Deterg.* **2009**, *12*, 165–172.
 (16) Borse, M.; Sharma, V.; Aswal, V. K.; Goyal, P. S.; Devi, S. *J. Colloid Interface Sci.* **2005**, *284*, 282–288.
 (17) Ao, M. Q.; Huang, P. P.; Xu, G. Y.; Yang, X. D.; Wang, Y. *J. Colloid Polym. Sci.* **2009**, *287*, 395–402.
 (18) Van Biesen, G.; Bottaro, C. S. *J. Chromatogr., A* **2008**, *1180*, 171–178.
 (19) Chen, Q. B.; Zhang, D. Z.; Li, R.; Liu, H. L.; Hu, Y. *Thin Solid Films* **2008**, *516*, 8782–8787.
 (20) Chen, L. F.; Li, Y.; Xie, H. Q. *J. Dispersion Sci. Technol.* **2008**, *29*, 1098–1102.
 (21) Klijn, J. E.; Stuart, M. C. A.; Scarzello, M.; Wagenaar, A.; Engberts, J. B. F. N. *J. Phys. Chem. B* **2006**, *110*, 21694–21700.
 (22) Menger, F. M.; Migulin, V. A. *J. Org. Chem.* **1999**, *64*, 8916–8921.
 (23) Murguía, M. C.; Grau, R. *J. Synlett* **2001**, 1229–1232.

SCHEME 1. Synthetic Strategy for the Synthesis of Cationic Gemini Surfactants Based on Pentaerythritol



SCHEME 2. Synthesis of Di-O-alkylpentaerythritols (9–12)



synthesis of the three series that contain variable numbers of methylene groups between the pentaerythritol quaternary center and the cationic center is shown in Scheme 1.

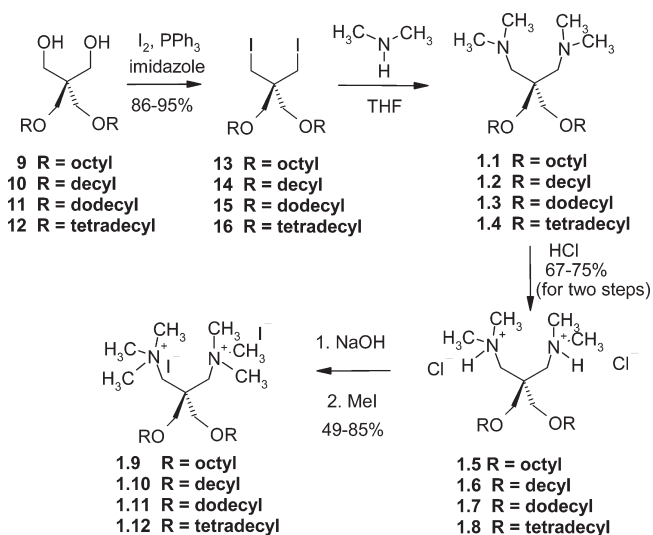
This simple strategy was selected because it can be used to prepare a wide variety of structures that will allow the thorough investigation of structure–function relationships. These investigations will be reported elsewhere.²⁴ Protection of two of the four pentaerythritol hydroxyls allows the incorporation of a variety of lipophilic groups through alkylation of the remaining two hydroxyls with use of alkyl halides. Here only linear alkyl halides were employed but other lipophilic groups could be used. Deprotection of the remaining two hydroxyls then allows their transformation into units bearing charged groups, trialkylammonium groups in this publication.

Synthesis of Alkylated Diols. As in the synthetic route used by Murguía and Grau,²³ a pentaerythritol derivative with two of the four hydroxyl groups protected was employed as the starting material, in this case, the readily available mono-*O*-benzylidenepentaerythritol (**4**).²⁵ This starting material was converted into di-*O*-alkylpentaerythritols (**9–12**) by double Williamson ether syntheses with linear alkyl bromides. If the reaction temperatures were kept close to 0 °C, the amounts of elimination byproducts from the alkyl bromides were negligible. Hydrogenolysis removed the benzylidene acetals in excellent yields, as shown in Scheme 2. In our hands, hydrogenolysis of the benzylidene acetals provided cleaner diols from benzylidene acetals **5** to **8** than did mild acid hydrolysis. Murguía and Grau²³ had used acid hydrolysis of cyclohexylidene acetals.

(24) Karpichev, Y.; Jahan, N.; Paul, N.; Tran, T.; Grindley, T. B.; Petropolis, C. J.; Marangoni, D. G. *Langmuir*, in preparation.

(25) Issidorides, C. H.; Gulen, R. C. *Monobenzalpenterythritol*. In *Organic Syntheses*; Rabjohn, N., Ed.; John Wiley and Sons: New York, 1963; Collect. Vol. IV, pp 679–681.

SCHEME 3. Synthesis of the Shortest Series of Cationic Gemini Surfactants (Series 1)



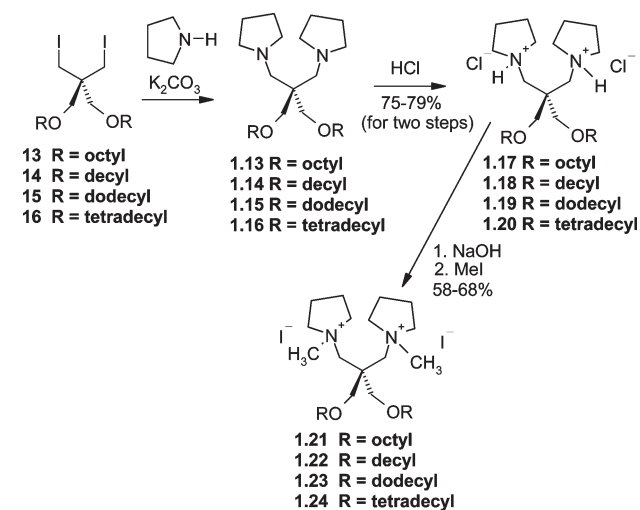
An alternative approach for the synthesis of diols **9–12** will be described later.²⁶

This publication describes the synthesis of five series of cationic pentaerythritol-based gemini surfactants. The series are numbered based on the distance the ionic group is from the quaternary carbon originating in pentaerythritol with the series having the shortest distance being series **1**. All compounds in each series are numbered with the series number followed by the number of the compound in the series (see schemes below).

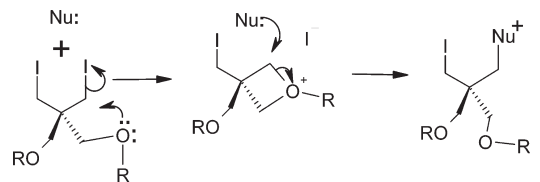
Synthesis of Series 1–3. The synthesis of the first series commenced with the conversion of the diols into diiodides with iodine, triphenylphosphine, and imidazole^{27,28} in excellent yields as shown in Scheme 3. Even though the iodine atoms are attached to primary carbons adjacent to quaternary centers, they can be displaced by nucleophiles. Linear nucleophiles, such as cyanide (see Scheme 6) or azide, also displaced iodide easily. Dimethylamine displaced iodide slowly at elevated temperatures in a sealed tube but we were unable to find conditions where the more branched nucleophiles, trimethylamine or sodium sulfite, could perform this displacement. The displacement products with dimethylamine were isolated as hydrochlorides in reasonable yields for the two steps (68–75%). The iodides can also be displaced with pyrrolidine (Scheme 4). These tertiary amines were alkylated with methyl iodide to give surfactant series **1** as shown in Schemes 3 and 4.

These nucleophilic displacements probably proceed by an S_N2 mechanism,^{29–31} even though S_N2 displacements of halides and tosylates in neopentyl derivatives are known to

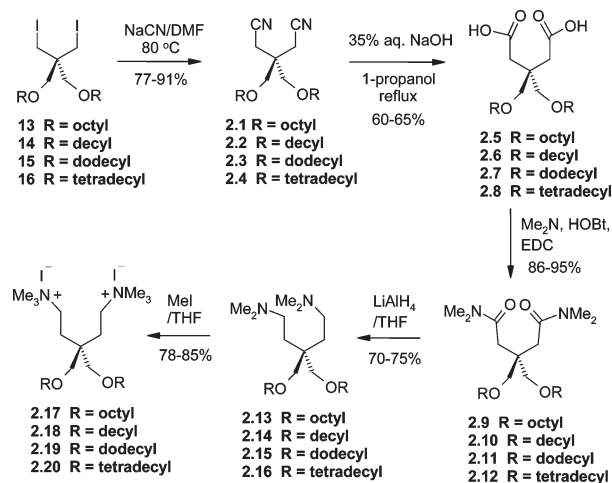
SCHEME 4. Synthesis of Cationic Gemini Surfactants by Displacement with Pyrrolidine



SCHEME 5. Neighbouring Group Participation in Displacements of Alkoxyneopentyl Iodides



SCHEME 6. Synthesis of the Second Series of Cationic Gemini Surfactants (Series 2)



occur slowly³² and mechanisms involving single electron transfer (S_{RN}1) are often considered for displacement of neopentyl halides,³³ particularly iodides.^{34,35} It is probable that S_N2 displacements in pentaerythritol systems are faster

(26) Tran, T.; Jahan, N.; Marangoni, D. G.; Grindley, T. B. *J. Org. Chem.*, in preparation.

(27) Garegg, P. J.; Johansson, R.; Ortega, C.; Samuelsson, B. *J. Chem. Soc., Perkin Trans. 1* **1982**, 681–683.

(28) Lubineau, A.; Malleron, A.; Le Narvor, C. *Tetrahedron Lett.* **2000**, *41*, 8887–8891.

(29) Anderson, P. H.; Stephenson, B.; Mosher, H. S. *J. Am. Chem. Soc.* **1974**, *96*, 3171–3177.

(30) DePuy, C. H.; Gronert, S.; Mullin, A.; Bierbaum, V. M. *J. Am. Chem. Soc.* **1990**, *112*, 8650–8655.

(31) Vayner, G.; Houk, K. N.; Jorgensen, W. L.; Brauman, J. I. *J. Am. Chem. Soc.* **2004**, *126*, 9054–9058.

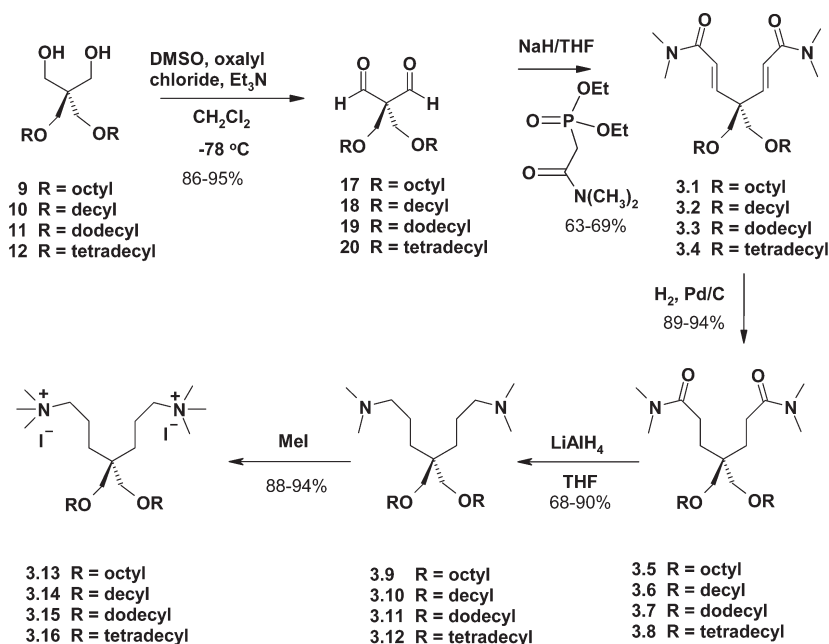
(32) Streitwieser, A. *Solvolytic displacement reactions*; McGraw-Hill: New York, 1962.

(33) Rossi, R. A.; Pierini, A. B.; Peñeñory, A. B. *Chem. Rev.* **2003**, *103*, 71–167.

(34) Ashby, E. C.; Argyropoulos, J. N. *J. Org. Chem.* **1985**, *50*, 3274–3283.

(35) Ashby, E. C.; Welder, C. O. *J. Org. Chem.* **1997**, *62*, 3542–3551.

SCHEME 7. Synthesis of Cationic Surfactants via Horner–Wadsworth–Emmons Reactions



than those in neopentyl systems because of neighboring group participation as shown in Scheme 5. Although participation by oxygen through four-membered-ring intermediates does not normally provide significant rate enhancement,^{36–39} when branching on the intervening atoms is present, significant rate enhancements have been observed.^{40,41} Dale and Fredriksen suggested that displacements of bromides by alkoxides from 2-bromo-2-methyl-1,3-dibromopropane proceed via four-membered-ring bromonium ion intermediates.⁴² We believe that the iodide displacements here follow the S_N2 mechanism both because neighboring group participation is possible and also because the dependency of ease of reaction on the steric bulk of the nucleophile fits what is expected for an S_N2 mechanism.

A second series of pentaerythritol-based cationic gemini surfactants with greater distances between head groups was synthesized as shown in Scheme 6. Cyanide displacement of the diiodides was followed by hydrolysis of the cyanides with sodium hydroxide in 2-propanol and conversion to the *N,N*-dimethylamides. Reduction and alkylation gave cationic surfactant series 2.

A third series of cationic surfactants was synthesized as shown in Scheme 7. The diols 9–12 were oxidized under Swern conditions⁴³ and the unstable dialdehydes were immediately used in Horner–Wadsworth–Emmons reactions

with the anion of diethyl *N,N*-dimethylcarbamoylmethylphosphonate. The latter compound was made by the reaction of triethyl phosphite with bromo-*N,N*-dimethylacetamide as performed by Barlett et al. with trimethyl phosphite.⁴⁴ Horner–Wadsworth–Emmons reactions using ylides stabilized by acetamido groups have been performed on a number of occasions,^{45–49} but never with dialdehydes, as far as we are aware. The conjugated amides were obtained exclusively as *trans* alkenes, as established from the magnitudes of the ³J_{H,H} values across the alkene (16 Hz). The alkenes were hydrogenated over 10% palladium/C then further reduced to tertiary amines with lithium aluminum hydride. Alkylation with methyl iodide yielded quaternary ammonium salts, the third series of gemini surfactants.

Cationic Gemini Surfactants Derived from Pentaerythritol Having Branching Chains Incorporating Ether Linkages. Two series of cationic gemini surfactants having ether linkages in the chains were prepared by Williamson ether syntheses. The dialkoxides derived from diols 9–12 react readily (50 °C) in DMF with 2-dimethylaminoethyl chloride because of neighboring group participation through three-membered-ring intermediates³⁹ to give dimethylamino derivatives, isolated as the hydrochlorides (see Scheme 1). Monosubstitution products were often present as minor impurities but were minimized by extending reaction times. Alkylation of the products with methyl iodide yielded cationic gemini surfactants of series 4.

(36) Jursic, B.; Ladika, M.; Sunko, D. E. *Gazz. Chim. Ital.* **1988**, *118*, 613–616.

(37) Winstein, S.; Henderson, R. B. *J. Am. Chem. Soc.* **1943**, *65*, 2196–2200.

(38) Winstein, S.; Ingraham, L. L. *J. Am. Chem. Soc.* **1952**, *74*, 1160–1164.

(39) Capon, B.; McManus, S. P. *Neighbouring Group Participation*; Plenum: New York, 1976; Vol. 1.

(40) Eliel, E. L.; Clawson, L.; Knox, D. E. *J. Org. Chem.* **1985**, *50*, 2707–2711.

(41) McManus, S. P.; Karaman, R. M.; Sedaghattherati, R.; Neamatimazraeh, N.; Hovanes, B. A.; Paley, M. S.; Harris, J. M. *J. Org. Chem.* **1987**, *52*, 2518–2522.

(42) Dale, J.; Fredriksen, S. B. *Acta Chem. Scand.* **1992**, *46*, 278–282.

(43) Omura, K.; Swern, D. *Tetrahedron* **1978**, *34*, 1651–1660.

(44) Bartlett, P. A.; Carruthers, N. I.; Winter, B. M.; Long, K. P. *J. Org. Chem.* **1982**, *47*, 1284–1291.

(45) Ordóñez, M.; Hernández-Fernández, E.; Montiel-Pérez, M.; Bautista, R.; Bustos, P.; Rojas-Cabrera, H.; Fernández-Zertuche, M.; García-Barradas, O. *Tetrahedron: Asymmetry* **2007**, *18*, 2427–2436.

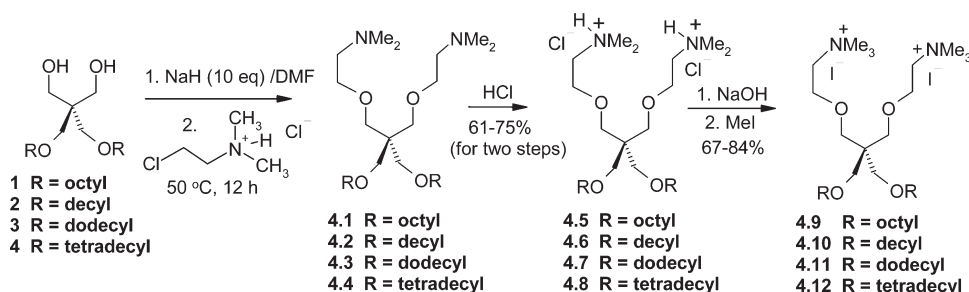
(46) Schauer, D. J.; Helquist, P. *Synthesis* **2006**, 3654–3660.

(47) Kojima, S.; Hidaka, T.; Ohba, Y. *Heteroatom Chem.* **2004**, *15*, 515–523.

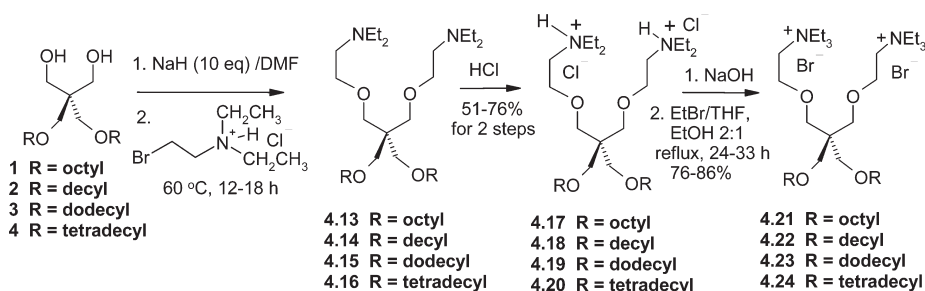
(48) Beck, B.; Picard, A.; Herdtweck, E.; Domling, A. *Org. Lett.* **2004**, *6*, 39–42.

(49) Petrova, J.; Momchilova, S.; Vassilev, N. G. *Phosphorus Sulfur Silicon* **2000**, *164*, 87–94.

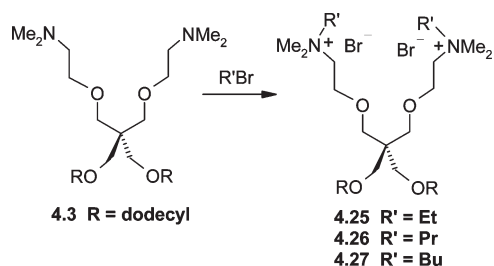
SCHEME 8. Synthesis of Pentaerythritol-Based Cationic Gemini Surfactants of Series 4 by Neighbouring-Group Assisted Double Williamson Ether Synthesis with 2-Dimethylaminoethyl Chloride



SCHEME 9. Synthesis of Pentaerythritol-Based Cationic Gemini Surfactants of Series 4 by Neighbouring-Group Assisted Double Williamson Ether Synthesis with 2-Diethylaminoethyl Bromide



SCHEME 10. Alkylation of Compound 4.3



Unfortunately, the Krafft temperatures of the longer chain members of these trimethylammonium derivatives were found to be greater than room temperature.²⁴ It is known that triethylammonium derivatives have lower Krafft temperatures than their trimethylammonium analogues.⁵⁰ Triethylammonium derivatives were synthesized in the same way as shown in Scheme 2 except that it was found necessary to run the Williamson ether syntheses at slightly higher temperatures, even though the leaving group in 2-diethylaminoethyl bromide is better than the chloride employed in Scheme 8. The diethylamino group must be a poorer neighboring group participator, probably because the larger group finds it more difficult to achieve the correct three-membered-ring geometry for participation.

An alternative approach to lowering the Krafft temperature was to alkylate the intermediate dimethylamines from the synthesis shown in Scheme 8 with different alkyl halides, as shown in Scheme 10.

A series of cationic surfactants with greater distances between head groups (series 5) was prepared by reacting the diol

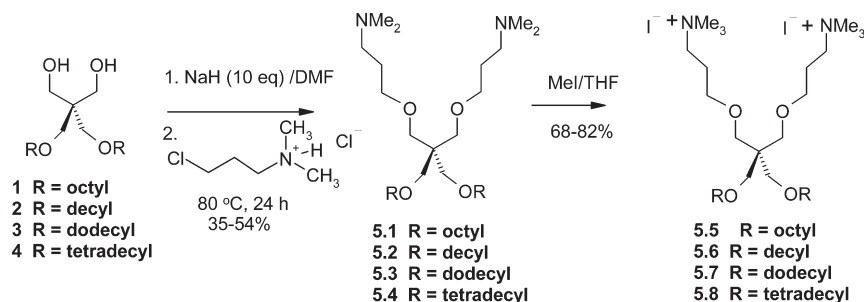
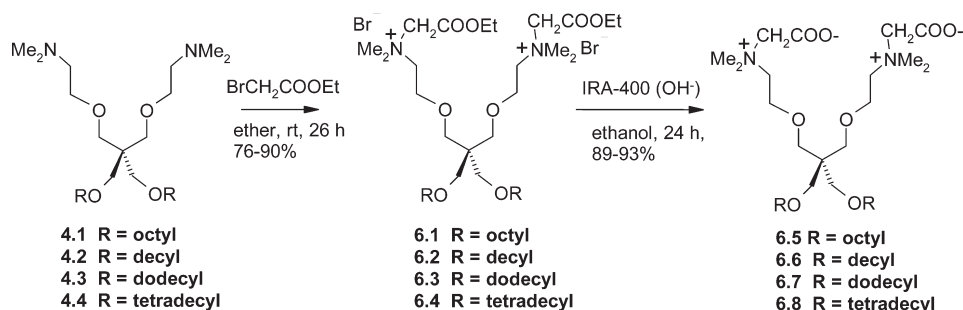
dialkoxides 1–4 with 3-dimethylaminopropyl chloride in DMF (Scheme 11). Here, neighboring group participation³⁹ involves four-membered-ring intermediates, which are known^{51–54} to be less effective for amines than the three-membered-ring intermediates used in the previous series. As a result, reaction temperatures had to be raised and reaction times increased. Reaction for shorter periods gave monosubstitution products.

Zwitterionic Gemini Surfactants. The normal procedures for the preparation of carboxymethyl derivatives of amines (betaines) use haloacetates or haloacetic acid as electrophiles. Attempts to perform these reactions on bisamines 4.1 to 4.4 always resulted in inseparable mixtures. It was found that the two-step procedure of Souiriti and Baboulène^{55,56} using ethyl bromoacetate as the electrophile resulted in pure surfactants, particularly when the ester hydrolysis was performed with an anion exchange resin as shown in Scheme 12.

All five series of cationic gemini surfactants as well as the series of zwitterionic gemini surfactants had good solubilities in water and had outstanding surfactant properties. These properties will be discussed in detail elsewhere.²⁴ CMCs of the compounds with C12 tails, 1.11, 2.19, 3.15, 4.11, 5.7, and 6.7, were 0.053, 0.041, 0.028, 0.054, 0.016, and 0.016 mM, respectively, as measured from the change in surface tension with concentration with a KRUSS K8 tensiometer. These CMCs are 1 to 2 orders of magnitude lower than most cationic gemini surfactants (see Table 1 in the review by Zana⁵⁷). C₂₀ values for these compounds are also promising.

(50) Davey, T. W.; Ducker, W. A.; Hayman, A. R.; Simpson, J. *Langmuir* 1998, 14, 3210–3213.

(51) Freundlich, H.; Kroepelin, H. *Z. Phys. Chem.* 1926, 122, 39–48.
(52) Dewey, C. S.; Bafford, R. A. *J. Org. Chem.* 1967, 32, 3108–3110.
(53) Bird, R.; Knipe, A. C.; Stirling, C. J. *J. Chem. Soc., Perkin Trans. 2* 1973, 1215–1220.
(54) Detar, D. F.; Luthra, N. P. *J. Am. Chem. Soc.* 1980, 102, 4505–4512.
(55) Souiriti, S.; Baboulène, M. *Synth. Commun.* 2001, 31, 9–18.
(56) Souiriti, S.; Baboulène, M. *Can. J. Chem.* 2001, 79, 1153–1158.
(57) Zana, R. Gemini Surfactants in Water. In *Gemini surfactants: Synthesis, Interfacial and Solution-phase Behaviour, and Applications*; Zana, R., Xia, J., Eds.; Marcel Dekker: New York, 2004; pp 109–140.

SCHEME 11. Synthesis of Pentaerythritol-Based Cationic Gemini Surfactants of Series 5 by Neighbouring-Group Assisted Double Williamson Ether Synthesis with 3-Dimethylaminopropyl Chloride

SCHEME 12. Synthesis of Zwitterionic Surfactants

Experimental Section

5,5'-Bis(octyloxymethyl)-2-phenyl-1,3-dioxane (5). A hexanes-washed sodium hydride oil dispersion (60% oil dispersion, 8.6 g, 0.22 mol, 2.0 equiv) was added in portions slowly to a stirred solution of mono-*O*-benzylidene-pentaerythritol²⁵ (**4**) (24.11 g, 0.1076 mol) in dry DMF (600 mL) under a nitrogen atmosphere. The stirred reaction mixture was cooled with an ice water bath for 1 h, then dried 1-bromooctane (46.76 mL, 51.90 g, 0.268 mol, 2.5 equiv) was added dropwise over 2 h. After the reaction mixture had been stirred 12 h at 0 °C, another addition of sodium hydride (4.5 g, 0.11 mol, 1.0 equiv) and 1-bromooctane (20 mL, 0.11 mol, 1.0 equiv) was made. If after the reaction mixture had been stirred a further 12 h at 0 °C TLC showed that some mono-*O*-octyl product was present, another identical addition was made. When all of the mono-*O*-octyl derivative had been consumed, the reaction mixture was quenched by the addition of methanol dropwise until foaming ceased. The reaction mixture was filtered and the solid was washed with dichloromethane (~150 mL). The combined filtrate and washings were concentrated and the residue was extracted with hexanes (300 mL, then 200 mL). The combined extracts were concentrated to an oily residue that was passed through a short silica gel column with hexanes, then 5% ethyl acetate/95% hexanes as eluents. The title compound (**5**) was a colorless oil (44.71 g, 85%); R_f 0.46 (hexanes:ethyl acetate 94:6); $^1\text{H NMR}$ (500.13 MHz) δ 0.88, 0.89 (2 t, 6H, $J = 6.5$ Hz, $2 \times \text{Me}$), 1.20–1.35 (br m, 20H, $10 \times \text{CH}_2$), 1.54, 1.57 (2 pentet, 4H, $J = 6.8$ Hz, $2 \text{ OCH}_2\text{CH}_2$), 3.22 (s, 2H, eq CCH_2O), 3.35 (t, 2H, $J = 6.5$ Hz, eq octyl OCH_2), 3.45 (t, 2H, $J = 6.6$ Hz, ax octyl OCH_2), 3.71 (s, 2H, ax OCH_2C), 3.88, 4.09 (2d, 4H, $J = 11.5$ Hz, H-4, H-4', H-6, H-6'), 5.42 (s, 1H, acetal H), 7.31–7.49 (m, 5H, Ph); $^{13}\text{C NMR}$ δ 138.5 (q Ph), 128.8 (para Ph), 128.3 (2C, mPh), 126.1 (2C, oPh), 101.7 (acetal C), 71.8 (eq OCH_2CH_2), 71.7 (ax OCH_2CH_2), 70.8 (eq OCH_2C), 70.2 (C-4 and C-6), 69.4 (ax OCH_2C), 38.9 (q C), 2×31.89 ($\text{CH}_2\text{CH}_2\text{CH}_3$), 29.68, 29.54, 29.51, 29.45, 2×29.34 (6 octyl CH_2), 26.22, 26.19 ($\text{CH}_2\text{CH}_2\text{CH}_2\text{O}$), 2×22.70 (CH_2CH_3), 14.3 (Me); HR ESI MS m/z calcd for $\text{C}_{28}\text{H}_{48}\text{O}_4\text{Na}$ ($M + \text{Na}$) 471.3445, found 471.3448.

2,2-Bis(octyloxymethyl)-1,3-propanediol (9). To a solution of compound **5** (10.02 g, 22.3 mmol) in ethyl acetate (100 mL) was added 10% Pd/C (Degussa type, 0.2 g). The mixture was stirred vigorously under atmospheric pressure of $\text{H}_2(\text{g})$ for 1 h. More 10% Pd/C (Degussa type, 0.5 g) was added and the solution was stirred until uptake of $\text{H}_2(\text{g})$ ceased (2 h). The mixture was filtered and the residue was washed with dichloromethane (50 mL), then dichloromethane containing 20% methanol (2×50 mL). The filtrate and washings were concentrated to a colorless solid: yield 6.89 g, 85%. Crystallization from 2-propanol gave colorless crystals: R_f 0.40 (dichloromethane: methanol 96:4); mp 35 °C; $^1\text{H NMR}$ δ 0.88 (t, 6H, $J = 6.9$ Hz, $2 \times \text{Me}$), 1.20–1.36 (br m, 20H, $10 \times \text{CH}_2$), 1.56 (pentet, 4H, $J = 6.8$ Hz, $2 \text{ OCH}_2\text{CH}_2$), 2.82 (t, 2H, $J = 6.1$ Hz, OH), 3.42 (t, 4H, $J = 6.5$ Hz, octyl OCH_2), 3.50 (s, 4H, OCH_2C), 3.65 (d, 4H, CH_2OH); $^{13}\text{C NMR}$ δ 73.1 ($\text{CCH}_2\text{OCH}_2\text{CH}_2$), 72.2 ($\text{CH}_2\text{CH}_2\text{OC}$), 65.5 (CH_2OH), 44.7 (q C), 31.9 ($\text{CH}_2\text{CH}_2\text{CH}_3$), 29.64 (OCH_2CH_2), 29.50, 29.35 (2 octyl CH_2), 26.3 ($\text{CH}_2\text{CH}_2\text{CH}_2\text{O}$), 22.8 (CH_2CH_3), 14.2 (Me); LR ESI MS m/z calcd for $\text{C}_{21}\text{H}_{45}\text{O}_4$ 361.33, found 361.1. Anal. Calcd for $\text{C}_{21}\text{H}_{44}\text{O}_4$: C, 69.95; H, 12.30. Found: C, 69.62; H, 12.68.

1,3-Diiodo-2,2-bis(octyloxymethyl)propane (13). Iodine (10.2 g, 0.0415 mol, 2.5 equiv), imidazole (2.73 g, 0.0415 mol, 2.5 equiv), and triphenylphosphine (8.94 g, 0.0353 mol, 2.2 equiv) were added to a solution of compound **9** (5.80 g, 0.0161 mol) in anhydrous toluene (200 mL) and the reaction mixture was refluxed for 3 h. More iodine was then added to consume excess triphenylphosphine and reflux was continued for 1 h. The cooled reaction mixture was stirred for 10 min each with saturated sodium bicarbonate (100 mL) and 10% aqueous sodium thiosulfate (200 mL) solutions. The organic layer was washed with water (3×50 mL), dried (MgSO_4), and concentrated. The residue was taken up in hexanes and the solution was passed through a short silica gel column. Concentration gave the title compound as a colorless oil: 7.89 g, 86%; R_f 0.34 (98:2 hexanes: dichloromethane); $^1\text{H NMR}$ δ 0.89 (t, 6H, $J = 6.3$ Hz, $2 \times \text{Me}$), 1.22–1.36 (br s, 20H, $10 \times \text{CH}_2$), 1.55 (pentet, 4H, $J = 6.1$ Hz, $2 \text{ OCH}_2\text{CH}_2$), 3.33 (s, 4H, CH_2I), 3.35 (s, 4H, OCH_2C), 3.42 (t, 4H,

octyl OCH₂); ¹³C NMR δ 71.7 (CH₂CH₂OC), 70.9 (CCH₂OCH₂C), 41.7 (q C), 32.0 (CH₂CH₂CH₃), 29.69, 29.56, 29.47 (3 octyl CH₂), 26.3 (CH₂CH₂CH₂O), 22.8 (CH₂CH₃), 14.3 (Me), 12.1 (CH₂); HR ESI MS *m/z* calcd for C₂₁H₄₃I₂O₂ (M + H) 581.1353, found 581.1351.

***N,N,N',N'*-Tetramethyl-2,2-bis(octyloxymethyl)-1,3-propanediaminium Dichloride (1.5).** Compound **13** (9.98 g, 17.2 mmol), dimethylamine in THF (2 M, 87 mL, 0.17 mol, 10 equiv), and potassium carbonate (5.9 g, 43 mmol, 2.5 equiv) were added to a sealed tube with the aid of THF (10 mL). The reaction mixture was stirred at 160–170 °C. After one week, all of the starting material had been consumed and the reaction mixture was filtered and the solvent was removed in vacuo at 35–40 °C to give a yellow oil, *N,N,N',N'*-tetramethyl-2,2-bis(octyloxymethyl)-1,3-propanediamine (**1.1**). The crude oil was taken up in dichloromethane (50 mL) and the resulting solution was shaken with ice cold 2 M HCl (75 mL). The aqueous layer was extracted with dichloromethane (2 × 50 mL), then the combined organic layers were washed with water (20 mL), dried (MgSO₄), and concentrated to give the title compound as a light yellow crystalline solid that was recrystallized from ethyl acetate:acetone 15:1 to give clear rectangular crystals: yield 5.62 g, 67%; mp 145 °C; *R_f* 0.29 on basic alumina (hexanes:ethyl acetate:methanol 96:4:0.4); ¹H NMR δ 0.88 ppm (t, 6H, *J* = 6.9 Hz, 2 × Me), 1.26–1.33 (br s, 20H, 10 × CH₂), 1.56 (pentet, 4H, *J* = 6.6 Hz, 2 OCH₂CH₂), 2.97 (s, 12H, 2 × N(CH₃)₂), 3.47 (t, 4H, *J* = 6.6 Hz, octyl OCH₂), 3.68 (s, 4H, OCH₂C), 3.79 (s, 4H, CH₂N), 11.78 (br s, HN); ¹³C NMR δ 71.7 (CH₂CH₂OC), 66.9 (CCH₂OCH₂C), 58.6 (CH₂N), 47.5 (N(CH₃)₂), 44.5 (q C), 31.8 (CH₂CH₂CH₃), 29.5, 29.3, 29.2 (3 octyl CH₂), 26.2 (CH₂CH₂CH₂O), 22.6 (CH₂CH₃), 14.1 (Me); HR ESI MS *m/z* calcd for C₂₅H₅₅N₂O₂ (M – H – 2Cl) 415.4264, found 415.4260.

***N,N,N,N',N',N'*-Hexamethyl-2,2-bis(octyloxymethyl)-1,3-propanediammonium Diiodide (1.9).** An aqueous NaOH solution (2 M, 30 mL) was added to salt **1.5** (4.44 g, 9.1 mmol) and the resulting mixture was extracted with dichloromethane (3 × 50 mL). The combined extracts were washed with water and dried (MgSO₄) and concentrated to a colorless syrup, *N,N,N',N'*-tetramethyl-2,2-bis(octyloxymethyl)-1,3-propanediamine (**1.1**): yield 2.45 g, 65%; *R_f* 0.39 on basic alumina (hexanes:ethyl acetate:methanol 96:4:0.4); ¹H NMR δ 0.88 ppm (t, 6H, *J* = 6.9 Hz, 2 × Me), 1.26–1.32 (br s, 20H, 10 × CH₂), 1.54 (pentet, 4H, *J* = 7.0 Hz, 2 OCH₂CH₂), 2.26 (s, 12H, 2 × N(CH₃)₂), 3.26 (s, 4H, 2 × NCH₂), 3.26 (s, 4H, OCH₂C), 3.33 (t, *J* = 6.5 Hz, 4H, octyl OCH₂); ¹³C NMR δ 71.2 (CH₂CH₂OC), 70.8 (CCH₂OCH₂C), 59.9 (CH₂N), 48.7 (N(CH₃)₂), 45.8 (q C), 32.0 (CH₂CH₂CH₃), 29.9, 29.6, 29.5, (3 octyl CH₂), 26.5 (CH₂CH₂CH₂O), 22.8 (CH₂CH₃), 14.2 (Me).

Methyl iodide (3.6 mL, 57.9 mmol, 10.0 equiv) was added to a stirred solution of compound **1.1** (2.4 g, 5.79 mmol) in dry THF (15 mL) and the resulting solution was refluxed for 24 h, then concentrated. The title compound, a light yellow crystalline solid, was recrystallized from ethyl acetate and acetone to give colorless crystals: yield 3.01 g, 75%; mp 160–162 °C; *R_f* on basic alumina 0.53 (chloroform:acetone:methanol 2:1:1); ¹H NMR δ 0.88 ppm (t, 6H, *J* = 6.9 Hz, 2 × Me), 1.27–1.29 (br s, 20H, 10 × CH₂), 1.60 (pentet, 4H, *J* = 6.6 Hz, 2 OCH₂CH₂), 3.51 (t, 4H, *J* = 6.7 Hz, octyl OCH₂), 3.65 (s, 18H, 6 × CH₃), 3.91 (s, 4H, OCH₂C), 4.45 (s, 4H, CH₂N); ¹³C NMR δ 72.2 (CH₂CH₂OC), 68.2 (CCH₂OCH₂C), 67.7 (CH₂N), 56.5 (N(CH₃)₃), 49.1 (q C), 31.9 (CH₂CH₂CH₃), 29.7, 29.4, 29.3, (octyl CH₂), 26.4 (CH₂CH₂CH₂O), 22.7 (CH₂CH₃), 14.2 (Me); HR ESI MS *m/z* calcd for C₂₇H₆₀N₂I₂O₂ (M – I) 571.3700, found 571.3702; calcd for C₅₄H₁₂₀N₄I₃O₄ (2M – I) 1269.6444, found 1269.6443.

1,3-Bis(1-azacyclopentyl)-2,2-bis(octyloxymethyl)propane Dihydrochloride (1.17). A stirred solution of compound **13** (18.0 g, 31.0 mmol) in pyrrolidine (100 mL) containing potassium carbonate (10.7 g, 31.0 mmol, 2.5 equiv) was refluxed under

nitrogen for 48 h, allowed to cool to rt, then filtered. The solid was washed with dichloromethane (2 × 10 mL) and the filtrate and washings were combined and diluted with dichloromethane (100 mL). The resulting solution was washed with water (3 × 100 mL), dried (MgSO₄), and concentrated at 30 °C to give crude 1,3-bis(1-azacyclopentyl)-2,2-bis(octyloxymethyl)propane (**1.13**): yield 14.20 g. This product was taken up in dichloromethane (100 mL) and the resulting solution was shaken with ice cold 2 M HCl (100 mL). The aqueous layer was extracted with dichloromethane (2 × 100 mL), then the combined organic layers were washed with water (20 mL), dried (MgSO₄), and concentrated to give the title compound as a light yellow crystalline solid that was recrystallized from hexanes:ethyl acetate 2:1 to give colorless crystals: yield 12.5 g, 75%; mp 124–125 °C, *R_f* 0.22 on basic alumina (hexanes:ethyl acetate:methanol 96:4:0.4); ¹H NMR δ 0.88 ppm (t, 6H, *J* = 6.9 Hz, 2 × Me), 1.26–1.31 (br s, 20H, 10 × CH₂), 1.55 (pentet, 4H, *J* = 6.6 Hz, 2 OCH₂CH₂), 2.06 (YY' part of AA'BB'XX'YY' pattern, 4H, ¹/₂ of 2 N(CH₂CH₂)₂), 2.25 (XX' part of AA'BB'XX'YY' pattern, 4H, ¹/₂ of 2 N(CH₂CH₂)₂), 3.21 (BB' part of AA'BB'XX'YY' pattern, 4H, ¹/₂ of 2 N(CH₂)₂), 3.46 (t, 4H, *J* = 6.6 Hz, octyl OCH₂), 3.59 (s, 4H, OCH₂C), 3.84 (s, 4H, CH₂N), 3.91 (AA' part of AA'BB'XX'YY' pattern, 4H, ¹/₂ of 2 N(CH₂)₂), 11.51 (br s, HN); ¹³C NMR δ 71.5 (CH₂CH₂OC), 67.5 (CCH₂OCH₂CH₂), 57.8 (NCH₂), 56.9 (CH₂N), 44.3 (q C), 31.7 (CH₂CH₂CH₃), 29.41, 29.25, 29.18 (3 octyl CH₂), 26.2 (CH₂CH₂CH₂O), 23.5 (NCH₂CH₂), 22.6 (CH₂CH₃), 14.0 (Me); HR ESI MS *m/z* calcd for C₂₉H₅₉N₂O₂ (M – H – 2Cl) 467.4577, found 467.4578.

1,3-Bis(1-methyl-1-azoniacyclopentyl)-2,2-bis(octyloxymethyl)propane Diiodide (1.21). An aqueous 2 M NaOH solution (50 mL) was added to compound **1.17** (12.5 g, 23.2 mmol) and the resulting mixture was extracted with dichloromethane (3 × 50 mL). The combined extracts were washed with water and dried (MgSO₄), then concentrated to give the free base, 1,3-bis(1-azacyclopentyl)-2,2-bis(octyloxymethyl)propane (**1.13**) as a light yellow syrup: yield 10.3 g, 72%; *R_f* 0.32 on basic alumina (hexanes:ethyl acetate:methanol 96:4:0.4); ¹H NMR δ 0.88 ppm (t, 6H, *J* = 6.8 Hz, 2 × Me), 1.27–1.34 (br s, 20H, 10 × CH₂), 1.53 (pentet, 4H, *J* = 6.7 Hz, 2 OCH₂CH₂), 1.68 (m, 8H, 2NCH₂CH₂), 2.48 (s, 4H, CH₂N), 2.56 (m, 8H, 2N(CH₂)₂), 3.27 (s, 4H, OCH₂C), 3.32 (t, 4H, *J* = 6.4 Hz, octyl OCH₂); ¹³C NMR δ 71.7 (CCH₂OCH₂CH₂), 71.1 (CH₂CH₂OC), 56.81 (CH₂N), 56.84 (NCH₂), 45.7 (q C), 31.9 (CH₂CH₂CH₃), 29.87, 29.55, 29.43 (3 octyl CH₂), 26.4 (CH₂CH₂CH₂O), 24.3 (NCH₂CH₂), 22.8 (CH₂CH₃), 14.1 (Me).

Methyl iodide (13.3 g, 21.3 mmol, 10 equiv) was added to a stirred solution of compound **1.13** (9.90 g, 21.3 mmol) in dry THF (50 mL). The resulting mixture was refluxed under nitrogen for 48 h, then concentrated. The title compound, a light brown crystalline solid, was recrystallized from ethyl acetate to give colorless crystals: yield 13 g, 81%; mp 92 °C; *R_f* 0.69 on basic alumina (chloroform:acetone:methanol:ammonia 2:2:1:0.5); ¹H NMR δ 0.89 ppm (t, 6H, *J* = 6.9 Hz, 2 × Me), 1.26–1.30 (br s, 20H, 10 × CH₂), 1.57 (pentet, 4H, *J* = 6.5 Hz, 2 OCH₂CH₂), 2.18 (YY' part of AA'BB'XX'YY' pattern, 4H, ¹/₂ of 2 N(CH₂CH₂)₂), 2.38 (XX' part of AA'BB'XX'YY' pattern, 4H, ¹/₂ of 2 N(CH₂CH₂)₂), 3.46 (s, 6H, 2 NCH₃), 3.49 (t, 4H, *J* = 6.6 Hz, octyl OCH₂), 3.96 (s, 4H, OCH₂C), 4.04 (m, 8H, 2 N(CH₂)₂), 4.63 (s, 4H, 2 CH₂N); ¹³C NMR δ 71.9 (CH₂CH₂OC), 68.3 (CCH₂OCH₂CH₂), 66.9 (NCH₂), 65.4 (CH₂N), 48.5 (CH₃N), 48.4 (q C), 31.8 (CH₂CH₂CH₃), 29.5, 29.3, 29.2 (3 octyl CH₂), 26.3 (CH₂CH₂CH₂O), 22.6 (CH₂CH₃), 21.1 (NCH₂CH₂), 14.1 (Me); HR ESI-MS *m/z* calcd for C₃₁H₆₄IN₂O₂ 623.4013 (M – I), found 623.4011.

3,3-Bis(octyloxymethyl)pentanedinitrile (2.1). Potassium cyanide (0.80 g, 12.0 mmol, 3.0 equiv) was added to a stirred solution of compound **13** (2.4 g, 4.1 mmol) in dry DMF

(25 mL). The resulting mixture was stirred at 80 °C for 24 h, and then allowed to cool to rt. A solid was deposited and the solution was decanted. The solid was washed with dichloromethane (2 × 10 mL). The combined solution and washings were concentrated to yellow oil that was taken up in dichloromethane (30 mL). The resulting solution was washed with water (3 × 25 mL), dried (MgSO₄), and concentrated to give the title compound as a light yellow oil: yield 1.3 g, 83%; *R_f* 0.42 (hexanes:ethyl acetate 9:1); ¹H NMR δ 0.88 (t, 6H, *J* = 6.9 Hz, 2 × Me), 1.23–1.33 (br s, 20H, 10 × CH₂), 1.55 (pentet, 4H, *J* = 7.0 Hz, 2 OCH₂CH₂), 2.57 (s, 4H, CH₂CN), 3.42 (s, 4H, OCH₂C), 3.44 (t, *J* = 6.5 Hz, 4H, octyl OCH₂); ¹³C NMR δ 116.7 (CN), 71.9 (CH₂CH₂OC), 70.8 (CCH₂OCH₂C), 41.3 (q C), 32.9 (CH₂CH₂CH₃), 29.45, 29.34 (2 octyl CH₂), 29.47 (OCH₂CH₂), 26.2 (CH₂CH₂CH₂O), 22.7 (CH₂CH₃), 21.7 (CH₂CN), 14.2 (Me); HR ESI MS *m/z* calcd for C₂₃H₄₂N₂O₂Na (M + Na) 401.3138, found 401.3152.

3,3-Bis(octyloxymethyl)pentanedioic Acid (2.5). A mixture of compound **2.1** (2.5 g, 5.61 mmol) in 1-propanol (40 mL) containing 35% NaOH (10 mL) was refluxed for 36 h. The reaction mixture was concentrated then the resulting aqueous reaction mixture was refluxed for another 24 h. The reaction mixture was cooled to 10 °C, then acidified by adding a dilute HCl solution until the pH was 5 (pH paper). The mixture was extracted with ethyl acetate (2 × 50 mL) and the combined organic layers were washed with water (2 × 30 mL) and brine (20 mL), dried (Na₂SO₄), and concentrated to give the crude product (**2.5**). The product was purified by flash column chromatography on silica gel, using a gradient changing from 5% EtOAc in hexanes to 15% EtOAc in hexanes as eluent. The product was obtained as a thick colorless syrup: yield 1.75 g (63%); *R_f* 0.5 (EtOAc:hexanes 1:1); ¹H NMR (CDCl₃) δ 0.88 (t, 6H, *J* = 6.5 Hz, CH₃), 1.24–1.31 (m, 20H, 10 × CH₂), 1.53 (pentet, 4H, *J* = 6.5 Hz, OCH₂CH₂), 2.61 (s, 4H, COCH₂), 3.40 (t, 4H, *J* = 6.5, OCH₂), 3.46 (s, 4H, OCH₂), 10.92 (br s, 2H, COOH); ¹³C NMR (CDCl₃) δ 176.8 (COOH), 73.2 (CCH₂O), 71.8 (OCH₂CH₂), 41.1 (q C), 37.5 (HOOCCH₂), 32.0 (CH₂CH₂CH₃), 29.60, 29.55, 29.42 (3 octyl CH₂), 26.3 (OCH₂CH₂CH₂), 22.8 (CH₃CH₂), 14.2 (CH₃); HR ESI MS *m/z* calcd for C₂₃H₄₃O₆ (M – 1) 415.3065, found 415.3042.

General Procedure for Formation of *N,N*-Dimethyl Amides: *N,N,N',N'*-Tetramethyl-3,3-bis(octyloxymethyl)pentanediamide (2.9). 1-Hydroxybenzotriazole (HOBT, 1.03 g, 7.69 mmol) and *N*-(3-dimethylamino-propyl)-*N'*-ethylcarbodiimide hydrochloride (EDC.HCl, 1.54 g, 8.07 mmol) were added to a stirred solution of diacid **2.5** (1.6 g, 3.9 mmol) and the reaction mixture was stirred for 1 h. Dimethylamine hydrochloride (1.25 g, 15.4 mmol) and triethylamine (2.7 g, 27 mmol) were added and the reaction mixture was stirred for another 24 h, then diluted with dichloromethane (50 mL). This mixture was washed with water (2 × 30 mL) and brine (20 mL), dried (Na₂SO₄), and concentrated. The residue was purified by flash column chromatography, using a gradient of 15% to 30% EtOAc in hexanes as eluent, yielding **2.9** as a viscous liquid: yield 1.63 g (91%); *R_f* 0.5 (ethyl acetate:hexanes 2:1); ¹H NMR (CDCl₃) δ 0.88 (t, 6H, *J* = 6.5 Hz, CH₃), 1.26–1.30 (m, 20H, 10 × CH₂), 1.51 (pentet, 4H, *J* = 6.5 Hz, OCH₂CH₂), 2.65 (s, 4H, COCH₂), 2.89 (s, 6H, NCH₃), 3.03 (s, 6H, NCH₃), 3.36 (t, 4H, *J* = 6.5 Hz, OCH₂), 3.53 (s, 4H, OCH₂); ¹³C NMR (CDCl₃) δ 172.4 (CO), 72.7 (CCH₂O), 71.4 (OCH₂CH₂), 42.1 (qC), 37.9 (NCH₃), 35.5 (NCH₃), 33.6 (NCOCH₂), 32.0 (CH₂CH₂CH₂), 29.87, 29.63, 29.51 (2 × 3 octyl CH₂), 26.4 (OCH₂CH₂CH₂), 22.8 (CH₃CH₂), 14.2 (CH₃); HR ESI MS *m/z* calcd for C₂₇H₅₄N₂O₄Na (M + Na) 493.3976, found 493.3966.

***N,N,N',N'*-Tetramethyl-3,3-bis(octyloxymethyl)-1,5-pentanediamine (2.13).** Diamide **2.9** (0.9 g, 1.91 mmol) was added dropwise to a stirred suspension of LiAlH₄ (0.29 g, 7.65 mmol) in THF (50 mL) at 0 °C, then the reaction mixture was stirred at rt for 6 h. Ethyl acetate (50 mL) was added dropwise, followed

by water (0.3 mL), then 1 M NaOH (0.3 mL). The mixture was filtered on a bed of Celite that was washed with hot ethyl acetate. The combined filtrate and washings were dried (Na₂SO₄), filtered, and concentrated to a residue that was purified by flash column chromatography. Elution with a gradient of 5% to 15% MeOH in dichloromethane gave **2.13** as a light brown liquid: yield 0.67 g (80%); *R_f* on basic alumina 0.46 (dichloromethane:methanol 96:4); ¹H NMR (CDCl₃) δ 0.88 (t, 6H, *J* = 7.0 Hz, CH₃), 1.22–1.38 (m, 20 H, 10 × CH₂), 1.43–1.54 (m, 8H, NCH₂CH₂, OCH₂CH₂), 2.21 (s, 12H, NCH₃), 2.27 (t, 4H, *J* = 8.0 Hz, NCH₂), 3.19 (s, 4H, OCH₂), 3.34 (t, 4H, *J* = 6.5 Hz, OCH₂); ¹³C NMR (CDCl₃) δ 73.8 (CCH₂O), 71.5 (OCH₂CH₂), 54.5 (NCH₂), 45.8 (NCH₃), 40.2 (qC), 32.0 (CH₃-CH₂CH₂), 30.3 (NCH₂CH₂), 29.89, 29.64, 29.50 (2 × 3 octyl CH₂), 26.5 (OCH₂CH₂CH₂), 22.8 (CH₃CH₂), 14.3 (CH₃); ESI MS *m/z* calcd for C₂₇H₅₈N₂O₂ (M + 1) 443.4571, found 443.4558.

***N,N,N',N'*-Hexamethyl-3,3-bis(octyloxymethyl)-1,5-pentanediammonium Diiodide (2.17).** A solution of methyl iodide (1.6 g, 11 mmol) and diamine **2.13** (0.50 g, 1.1 mmol) in THF (20 mL) was refluxed for 36 h, then concentrated. The solid residue was purified by flash column chromatography with 10% methanol in dichloromethane as eluent to give the title product as an off-white solid: yield 0.70 g (85%); mp 223–225 °C; *R_f* 0.5 on basic alumina (8% methanol in dichloromethane); ¹H NMR (CDCl₃) δ 0.88 (t, 6H, *J* = 7.0 Hz, CH₃), 1.22–1.28 (m, 20 H, 10 × CH₂), 1.45 (t, 4H, *J* = 6.0 Hz, OCH₂CH₂), 1.83 (AA' part of AA'XX' pattern, 4H, NCH₂CH₂), 3.13 (s, 4H, OCH₂), 3.15 (s, 18H, NCH₃), 3.18 (t, 4H, *J* = 7.0 Hz, OCH₂), 3.73 (XX part of AA'XX' pattern, 4H, NCH₂); ¹³C NMR (CDCl₃) δ 71.7 (CCH₂O), 71.5 (OCH₂CH₂), 62.8 (CH₂N(CH₃)₃), 54.2 (NCH₃), 41.6 (qC), 32.0 (CH₂CH₂CH₂), 29.82, 29.58, 29.50 (3 octyl CH₂), 26.6 (OCH₂CH₂CH₂), 24.6 (NCH₂CH₂), 22.8 (CH₃-CH₂), 14.3 (CH₃); HR ESI MS *m/z* calcd for C₂₉H₆₄IN₂O₂ (M – 1) 599.4007, found 599.3993.

***N,N,N',N'*-Tetramethyl-4,4-bis(octyloxymethyl)-2,5-heptanedienediamide (3.1).** A solution of dry dimethyl sulfoxide (DMSO) (0.47 g, 6.11 mmol) in dichloromethane (2 mL) was added dropwise to a stirred solution of oxalyl chloride (0.38 g, 3.0 mmol) in dichloromethane (5 mL) at –78 °C. After the reaction mixture had been stirred for 30 min, a solution of diol **9** (0.50 g, 1.4 mmol) was added and the reaction mixture was stirred for 1.5 h at –78 °C, then Et₃N (0.98 g, 9.7 mmol) was added slowly. The reaction mixture was stirred for 30 min, allowed to warm to rt, then quenched by addition of a saturated NH₄Cl solution (10 mL). The reaction mixture was extracted with dichloromethane (3 × 50 mL), and the combined organic layers were washed with 2 M HCl (5 mL), water (2 × 5 mL), and brine (5 mL), then dried (Na₂SO₄) and concentrated to give 2,2-bis(octyloxymethyl)propanedial (**17**) as a colorless viscous oil: yield 0.47 g, 95%; *R_f* 0.56 (hexanes:ethyl acetate 8:2); ¹H NMR δ 0.88 (t, 6H, *J* = 7.0 Hz, 2 × Me), 1.26–1.32 (br s, 20H, 10 × CH₂), 1.51 (p, 4H, *J* = 7.2 Hz, 2 OCH₂CH₂), 3.42 (t, 4H, *J* = 6.5 Hz, decyl OCH₂), 3.87 (s, 4H, OCH₂C), 9.74 (s, 2H, CHO); ¹³C NMR δ 199.4 (CHO), 72.3 (CH₂CH₂OC), 68.6 (OCH₂C), 43.8 (q C), 31.7 (CH₂CH₂CH₃), 29.76, 29.62, 29.48, 29.44, 29.37 (5 decyl CH₂), 26.12 (CH₂CH₂CH₂O), 22.8 (CH₂CH₃), 14.2 (Me); LR ESI *m/z* calcd for C₂₁H₄₀O₄Na·MeOH 411.31, found 411.3; for C₂₁H₄₀O₄Na·2MeOH 443.33, found 443.3; for 2 C₂₁H₄₀O₄ + Na + H₂O 753.54, found 753.6.

Diethyl *N,N*-dimethylcarbamoylmethylphosphonate^{44,58} (4.1 g, 18 mmol) in THF (10 mL) was added in portion to a stirred suspension of NaH (0.45 g, 18 mmol) in THF (80 mL) at rt and the reaction mixture was stirred for 2 h, then cooled to 0 °C. A solution of dialdehyde **17** (1.6 g, 4.5 mmol) in THF

(58) Lomakina, V. I.; Mandel'baum, Y.; Mel'nikov, N. N. *Zh. Obshch. Khim.* **1966**, *36*, 447–449.

(10 mL) was added and the reaction mixture was stirred for 24 h at rt. A saturated aqueous ammonium chloride solution (20 mL) was added to the reaction mixture and then the volatile organic components were removed by concentration. The resulting solution was extracted with ethyl acetate (3 × 30 mL). The combined organic layers were washed with water (2 × 20 mL) and brine (20 mL), dried (Na₂SO₄), filtered, and concentrated. The residue was purified by flash column chromatography, using a gradient of 80% to 90% EtOAc in hexanes as eluent, yielding **3.1** as a viscous liquid: yield 1.4 g (63%); *R_f* 0.35 (dichloromethane:methanol 94:6); ¹H NMR δ 0.88 (t, 6H, *J* = 7 Hz, 2 × Me), 1.26–1.34 (br s, 20H, 10 × CH₂), 1.53 (pentet, 4H, *J* = 7 Hz, 2 OCH₂CH₂), 2.99 (s, 3H, NCH₃), 3.05 (s, 3H, NCH₃), 3.39 (t, 4H, *J* = 6.5 Hz, decyl OCH₂), 3.49 (s, 4H, OCH₂C), 6.36 (d, 2H, *J* = 16 Hz, COCHCH), 6.86 (d, 2H, *J* = 16 Hz, COCHCH); ¹³C NMR δ 166.8 (C=O), 145.3 (CH=CHC), 121.9 (COCH=), 72.9 (CH₂CH₂OC), 71.9 (OC-H₂C), 48.9 (q C), 37.5 (NCH₃), 35.8 (NCH₃), 32.0 (CH₂-CH₂CH₃), 29.77, 29.61, 29.45 (3 octyl CH₂), 26.4 (CH₂CH₂-CH₂O), 22.8 (CH₂CH₃), 14.2 (Me); HR ESI MS *m/z* calcd for C₂₉H₅₄N₂O₄Na (M + Na) 517.3976, found 517.3971.

***N,N,N',N'*-Tetramethyl-4,4-bis(octyloxymethyl)heptanediamide (3.5)**. A mixture of **3.1** (0.5 g, 1.0 mmol) and 10% Pd/C wet Degusa type catalyst (50 mg) in ethyl acetate (50 mL) was stirred under H₂ at atmospheric pressure for 24 h. The reaction mixture was filtered with a Celite bed and the filtrate was concentrated to give compound **3.5** as a colorless liquid: yield 0.46 g (91%); *R_f* 0.5 (dichloromethane:methanol 95:5); ¹H NMR δ 0.88 (t, 6H, *J* = 6.5 Hz, 2 × Me), 1.25–1.31 (br s, 20H, 10 × CH₂), 1.50 (pentet, 4H, *J* = 7 Hz, 2 OCH₂CH₂), 1.61 (4H, AA'XX' pattern, CCH₂), 2.32 (4H, AA'XX' pattern, COCH₂), 2.99 (s, 3H, NCH₃), 3.07 (s, 3H, NCH₃), 3.22 (s, 4H, OCH₂C), 3.34 (t, 4H, *J* = 6.5 Hz, decyl OCH₂); ¹³C NMR δ 173.8 (C=O), 73.9 (CH₂CH₂OC), 71.7 (OCH₂C), 40.6 (qC), 37.4 (NCH₃), 35.6 (NCH₃), 32.0 (CH₂CH₂CH₃), 29.90, 29.64, 29.48 (3 octyl CH₂), 28.04, 27.94 (COCH₂CH₂, COCH₂), 26.5 (CH₂CH₂CH₂O), 22.8 (CH₂CH₃), 14.3 (Me); HR ESI MS *m/z* calcd for C₂₉H₅₈N₂O₄Na (M + Na) 521.4289, found 521.4278.

***N,N,N',N'*-Tetramethyl-4,4-bis(octyloxymethyl)-1,7-heptanediamine (3.9)**. Diamide **3.5** (0.6 g, 1.2 mmol) was added dropwise to a stirred suspension of LiAlH₄ (0.18 g, 4.8 mmol) in THF at 0 °C. The reaction mixture was stirred at rt for 6 h, then the excess of LAH was decomposed by dropwise addition of ethyl acetate (50 mL), water (0.3 mL), then 1 M NaOH (0.3 mL) at 10 °C. The mixture was filtered on a bed of Celite, which was then washed with hot ethyl acetate. The combined filtrate and washings were dried (Na₂SO₄), then concentrated to a residue that was purified by flash column chromatography. Elution with a gradient of 5% to 15% MeOH in dichloromethane gave the title compound as a light brown liquid: yield 0.45 g (80%); *R_f* on basic alumina 0.71 (dichloromethane:methanol 94:6); ¹H NMR (CDCl₃) δ 0.88 (t, 6H, *J* = 7.0 Hz, CH₃), 1.21–1.33 (m, 24 H, 10 octyl CH₂, 2 CCH₂), 1.37–1.43 (m, 4H, NCH₂CH₂), 1.51 (pentet, 4H, *J* = 7 Hz, OCH₂CH₂), 2.201 (t, 4H, *J* = 7.5 Hz, NCH₂), 2.206 (s, 12H, NCH₃), 3.17 (s, 4H, OCH₂), 3.33 (t, 4H, *J* = 6.5 Hz, OCH₂); ¹³C NMR (CDCl₃) δ 73.5 (CCH₂O), 71.5 (OCH₂), 60.9 (NCH₂), 45.7 (NCH₃), 41.0 (qC), 32.0 (CH₂CH₂CH₃), 29.85, 29.76, 29.65, 29.50 (3 octyl CH₂, CCH₂), 26.5 (OCH₂CH₂CH₂), 22.8 (CH₂CH₃), 21.45 (NCH₂CH₂), 14.3 (Me); HR ESI MS *m/z* calcd for C₂₉H₆₃N₂O₂ (M + 1) 471.4884, found 471.4885.

***N,N,N',N',N'*-Hexamethyl-4,4-bis(octyloxymethyl)-1,7-heptanediammonium Diiodide (3.13)**. Methyl iodide (1.51 g, 10.6 mmol) was added to a stirred solution of amine **3.9** (0.5 g, 1.0 mmol) in THF (30 mL). The reaction mixture was refluxed for 12 h, then concentrated. The solid residue was purified by flash column chromatography with 10% methanol in dichloromethane as eluent to give the title compound as an off-white

solid: yield 0.75 g (94%); mp 233–236 °C; *R_f* 0.5 on basic alumina (7% methanol in dichloromethane); ¹H NMR (CDCl₃) δ 0.88 (t, 6H, *J* = 7.0 Hz, CH₃), 1.23–1.31 (m, 20 H, 10 × CH₂), 1.43 (m, 4H, *J* = 8.2 Hz NCH₂CH₂CH₂), 1.51 (pentet, 4H, *J* = 6.5 Hz, 2 × OCH₂CH₂), 1.88 (m, 4H, NCH₂-CH₂), 3.21 (s, 4H, OCH₂), 3.36 (t, 4H, *J* = 6.5 Hz, OCH₂), 3.44 (s, 18H, NCH₃), 3.73 (m, 2H, NCH₂); ¹³C NMR (CDCl₃) δ 72.5 (CCH₂O), 71.6 (OCH₂), 67.8 (NCH₂), 54.5 (NCH₃), 41.4 (qC), 32.0 (CH₂CH₂CH₃), 29.82, 29.62, 29.53 (octyl CH₂), 26.7 (CCH₂), 26.5 (OCH₂CH₂CH₂), 22.8 (CH₃CH₂), 17.8 (NCH₂CH₂), 14.3 (Me); HR ESI MS *m/z* calcd for C₃₁H₆₈N₂O₂ (M + 1) 627.4320, found 627.4267.

***N,N,N',N'*-Tetramethyl-5,5-bis(octyloxymethyl)-3,7-dioxo-1,9-nonanediaminium Dichloride (4.5)**. Sodium hydride (3.36 g, 0.14 mol, 10 equiv) was added slowly to a stirred solution of 2,2-dioctyloxymethyl-1,3-propanediol (**1**) (5.05 g, 0.014 mol) in DMF (500 mL) under nitrogen gas at rt and the mixture was stirred vigorously for 1 h. 2-(Dimethylamino)ethyl chloride hydrochloride (8.08 g, 0.05 mol, 4 equiv) was added and the reaction mixture was stirred at 50 °C under an N₂ atmosphere for 12 h, then quenched with methanol. The mixture was filtered and concentrated. The residue was taken up in diethyl ether (50 mL) and the resulting solution was washed with brine (50 mL), dried (MgSO₄), and concentrated at 30–35 °C to give *N,N,N',N'*-tetramethyl-5,5-bis(octyloxymethyl)-3,7-dioxo-1,9-nonanediamine (**4.1**) as an orange oil. The crude product was taken up in dichloromethane (50 mL) and the resulting solution was shaken with ice cold 2 M HCl (30 mL). The aqueous layer was diluted with brine and this solution was extracted with dichloromethane (5 × 30 mL). The combined organic layers were dried (MgSO₄) and concentrated to give the title compound (**4.5**) as a light yellow solid that was crystallized from ethyl acetate and acetone to give colorless crystals: yield 4.90 g, 61%; mp 150–152 °C; *R_f* on basic alumina 0.47 (dichloromethane:ethanol 96:4); ¹H NMR δ 0.88 (t, 6H, *J* = 6.8 Hz, 2 × Me), 1.27 (br s, 20H, 10 × CH₂), 1.50 (pentet, 4H, *J* = 6.3 Hz, 2 OCH₂CH₂), 2.92 (s, 12H, 2 × N(CH₃)₂), 3.33 (t, 4H, *J* = 6.7 Hz, octyl OCH₂), 3.34 (s over broad pattern, 8H, octylOCH₂C and OCH₂CH₂N), 3.51 (s, 4H, N(CH₂)₂OCH₂C), 3.90 (XX' part of AA'XX' pattern, 4H, OCH₂CH₂N), 12.0 (br s, 2H, NH); ¹³C NMR δ 71.7 (CH₂CH₂OC), 70.6 (CCH₂O (CH₂)₂N), 69.5 (CCH₂O octyl), 65.8 (OCH₂CH₂N), 56.7 (NCH₂CH₂), 45.1 (q C), 43.6 (N(CH₃)₂), 32.0 (CH₂CH₂CH₃), 29.7, 29.5, 29.3 (octyl CH₂), 26.2 (CH₂CH₂CH₂O), 22.7 (CH₂CH₃), 14.2 (Me); HR ESI MS *m/z* calcd for C₂₉H₆₃N₂O₄ (M + H) 503.4788, found 503.4784.

***N,N,N',N',N',N'*-Hexamethyl-5,5-bis(octyloxymethyl)-3,7-dioxo-1,9-nonanediammonium Diiodide (4.9)**. Salt **4.5** (4.1 g, 7.1 mmol) was dissolved in a NaOH solution (2 M, 30 mL) and the resulting mixture was extracted with diethyl ether (2 × 30 mL). The combined extracts were washed with brine (10 mL), dried (MgSO₄), and concentrated to give a light yellow syrup, *N,N,N',N'*-tetramethyl-5,5-bis(octyloxymethyl)-3,7-dioxo-1,9-nonanediamine (**4.1**): yield 3.20 g, 89%; *R_f* on basic alumina 0.44 (chloroform:ethanol 98:2); ¹H NMR δ 0.88 (t, 6H, *J* = 6.9 Hz, 2 × Me), 1.25–1.33 (br m, 20H, 10 × CH₂), 1.51 (pentet, 4H, *J* = 6.8 Hz, 2 × OCH₂CH₂), 2.26 (s, 12H, 2 × N(CH₃)₂), 2.49 (t, 4H, *J* = 5.8 Hz, OCH₂CH₂N), 3.35 (t, 4H, *J* = 6.5 Hz, octyl OCH₂), 3.36 (s, 4H, octylOCH₂C), 3.39 (s, 4H, NCH₂CH₂OCH₂C), 3.49 (t, 4H, *J* = 6.0 Hz, OCH₂CH₂N); ¹³C NMR δ 71.9 (CH₂CH₂OC), 70.5 (NCH₂CH₂OCH₂), 70.3 (OCH₂CH₂N), 69.8 (CCH₂O octyl), 58.8 (OCH₂CH₂N), 46.1 (N(CH₃)₂), 45.6 (q C), 32.0 (CH₂CH₂CH₃), 29.70, 29.57, 29.54 (3 octyl CH₂), 29.40 (OCH₂CH₂), 26.3 (CH₂CH₂CH₂O), 22.8 (CH₂CH₃), 14.2 (Me); LR ESI MS *m/z* calcd for C₂₉H₆₃N₂O₄ (M + H) 503.47, found 503.4; calcd for M + Na 525.46, found 525.5.

Compound **4.1** (7.49 g, 0.0149 mol) was shaken with methyl iodide (8.28 g, 0.0584 mol, 4 equiv) for 2 min, then dichloromethane (100 mL) was added and shaking was continued for 5 min. The reaction mixture was concentrated to a yellow solid, which was washed with acetone, then crystallized from toluene: ethanol 10:1 to give colorless crystals: yield 10.17 g, 87%; recrystallized from ethyl acetate:methanol; R_f on basic alumina 0.54 (butanol:water:methanol 20:5:2); mp softens 180 °C, melts 188–189 °C; $^1\text{H NMR}$ δ 0.89 (t, 6H, $J = 6.9$ Hz, $2 \times \text{Me}$), 1.28–1.32 (br s, 20H, $10 \times \text{CH}_2$), 1.51 (pentet, 4H, $J = 6.3$ Hz, $2 \text{ OCH}_2\text{CH}_2$), 3.30 (s, 4H, octylOCH₂C), 3.33 (t, 4H, $J = 6.6$ Hz, octyl OCH₂), 3.51 (s, 4H, N(CH₂)₂OCH₂C), 3.54 (s, 18H, $2 \times \text{N}(\text{CH}_3)_3$), 3.94 (br s, 4H, OCH₂), 4.02 (br m, 4H, CH₂N); $^{13}\text{C NMR}$ δ 71.8 (CH₂CH₂OC), 70.9 (CCH₂O(CH₂)₂N), 69.4 (CCH₂Ooctyl), 65.8 (CH₂N), 65.4 (OCH₂CH₂N), 54.9 (N(CH₃)₃), 45.2 (q C), 31.9 (CH₂CH₂CH₃), 29.66, 29.41, 29.32 (3 octyl CH₂), 29.46 (OCH₂CH₂), 26.2 (CH₂CH₂CH₂O), 22.7 (CH₂CH₃), 14.2 (Me); LR ESI MS m/z calcd for C₃₁H₆₈N₂O₄I (M – I) 659.45, found 659.1. Anal. Calcd for C₃₁H₆₈N₂O₄I₂: C, 47.33; H, 8.71; N, 3.56. Found: C, 47.34; H, 8.51; N, 3.29.

***N,N,N',N'*-Tetraethyl-5,5-bis(octyloxymethyl)-3,7-dioxa-1,9-nonanediaminium Dihydrochloride (4.17)**. Sodium hydride (6.10 g, 0.15 mol, 10 equiv) was added slowly to a stirred solution of 2,2-dioctyloxymethyl-1,3-propanediol (**9**) (5.50 g, 0.015 mol) in THF (500 mL) under N₂ gas at rt. When foaming ceased, the mixture was stirred vigorously at 60 °C for 1 h. The reaction mixture was cooled to rt, then 2-bromo-*N,N*-diethylethylamine hydrobromide (15.95 g, 0.061 mol, 4.0 equiv) was added. The reaction mixture was stirred at 60 °C under N₂ gas for 12 h, then quenched with methanol. The reaction mixture was filtered and the filtrate concentrated to a syrupy residue. The residue was taken up in diethyl ether (50 mL) and the resulting solution was washed with brine (50 mL), dried (MgSO₄), and concentrated at 30–35 °C to give crude *N,N,N',N'*-tetraethyl-5,5-bis(octyloxymethyl)-3,7-dioxa-1,9-nonanediamine (**4.13**). The crude product was taken up in dichloromethane (50 mL) and the resulting solution was shaken with ice cold 2 M HCl (30 mL). The aqueous layer was diluted with brine (20 mL) and this solution was extracted with dichloromethane (5 \times mL). The combined organic layers were dried (MgSO₄) and concentrated to give the title compound (**4.17**) as a colorless solid, which was crystallized from ethyl acetate and acetone to give colorless granules: yield 7.20 g, 75%; mp 155 °C; R_f 0.5 (dichloromethane: ethanol 96:4); $^1\text{H NMR}$ δ 0.88 (t, 6H, $J = 6.8$ Hz, $2 \times \text{Me}$), 1.27 (br s, 20H, $10 \times \text{CH}_2$), 1.42 (t, 12H, $J = 7.2$ Hz, $4 \times \text{Me}$), 1.51 (pentet, 4H, $J = 6.3$ Hz, $2 \text{ OCH}_2\text{CH}_2$), 3.21 (very br AB part of ABX₃ pattern, 8H, NCH₂CH₃), 3.26 (br t, 4H, NCH₂CH₂O), 3.31 (s, 4H, octyl OCH₂C), 3.33 (t, 4H, $J = 6.6$ Hz, octyl OCH₂), 3.44 (s, 4H, N(CH₂)₂OCH₂C), 3.91 (t, 4H, $J = 4.3$ Hz, OCH₂CH₂N), 12.0 (br s, 2H, NH); $^{13}\text{C NMR}$ δ 71.7 (CH₂CH₂OC), 70.6 (CCH₂O(CH₂)₂N), 69.4 (CCH₂O octyl), 65.8 (OCH₂CH₂N), 50.9 (NCH₂CH₂), 47.3 (NCH₂CH₃), 45.1 (q C), 32.0 (CH₂CH₂CH₃), 29.6, 29.5, 29.3 (octyl CH₂), 26.2 (CH₂CH₂CH₂O), 22.7 (CH₂CH₃), 14.1 (Me), 8.8 (Me); HR ESI MS m/z calcd for C₃₃H₇₂N₂O₄/2 (M + 2H/2) 280.2741, found 280.2741.

***N,N,N',N'*-Hexaethyl-5,5-bis(octyloxymethyl)-3,7-dioxa-1,9-nonanediaminium Dibromide (4.21)**. Salt **4.17** (1.44 g, 2.28 mmol) was dissolved in a NaOH solution (2 M, 15 mL). The resulting mixture was extracted with diethyl ether (3 \times 5 mL) to yield a colorless syrup of *N,N,N',N'*-tetraethyl-5,5-bis(octyloxymethyl)-3,7-dioxa-1,9-nonanediamine (**4.13**), yield 1.08 g, 85%; R_f 0.43 on basic alumina (dichloromethane:ethanol 98:2); $^1\text{H NMR}$ δ 0.88 (t, 6H, $J = 6.8$ Hz, $2 \times \text{Me}$), 1.03 (t, $J = 7.2$ Hz, 12H, $4 \times \text{Me}$) 1.28 (br s, 20H, $10 \times \text{CH}_2$), 1.51 (pentet, 4H, $J = 6.8$ Hz, $2 \text{ OCH}_2\text{CH}_2$), 2.57 (q, 8H, $J = 7.1$ Hz, $2 \times \text{N}(\text{CH}_2\text{CH}_3)_2$), 2.65 (t, 4H, $J = 6.2$ Hz, $2\text{NCH}_2\text{CH}_2$), 3.35 (t, $J = 6.5$ Hz, 4H, octyl OCH₂), 3.35 (s, 4H, decylOCH₂C), 3.38

(s, 4H, CCH₂O(CH₂)₂N), 3.47 (t, $J = 6.3$ Hz, 4H, $2 \text{ OCH}_2\text{CH}_2$); $^{13}\text{C NMR}$ δ 71.6 (CH₂CH₂OC), 70.4 (CCH₂O(CH₂)₂N), 70.4 (CH₂CH₂N), 69.8 (CCH₂O octyl), 52.1 (NCH₂CH₂), 47.8 (NCH₂CH₃), 45.4 (q C), 32.0 (CH₂CH₂CH₃), 29.8, 29.6, 29.5, 29.3 (octyl CH₂), 26.3 (CH₂CH₂CH₂O), 22.8 (CH₂CH₃), 14.2 (Me), 12.1 (CH₂CH₃).

Ethyl bromide (98%, 2.78 mL, 37.3 mmol, 20.0 equiv) was added to a stirred solution of compound **4.13** (1.04 g, 1.86 mmol) in a mixture of THF and ethanol (6 mL) (2:1). Potassium carbonate (0.5 g, 3.7 mmol, 2 equiv) was added and the resulting mixture was refluxed for 26 h, cooled to rt, and filtered, then the filtrate was concentrated to give the title compound (**4.21**) as a colorless sticky solid (1.92 g). The salt precipitated from ethyl acetate containing a few drops of methanol: yield 1.13 g, 78%; mp 157 °C; R_f 0.53 on basic alumina (butanol:water:methanol 20:5:2); $^1\text{H NMR}$ δ 0.88 (t, 6H, $J = 6.9$ Hz, $2 \times \text{Me}$), 1.28 (br s, 20H, $10 \times \text{CH}_2$), 1.41 (t, $J = 7.2$ Hz, 12H, $6 \times \text{Me}$), 1.51 (pentet, 4H, $J = 6.5$ Hz, $2 \text{ OCH}_2\text{CH}_2$), 3.28 (s, 4H, octyl OCH₂C), 3.33 (t, $J = 6.6$ Hz, 4H, octyl OCH₂), 3.47 (s, 4H, CCH₂O(CH₂)₂N), 3.47 (q, 12H, $J = 7.2$ Hz, $2 \text{ N}(\text{CH}_2\text{CH}_3)_2$), 3.79 (AA' part of AA'BB' pattern, 4H, $2 \text{ NCH}_2\text{CH}_2$), 3.94 (BB' part of AA'BB' pattern, 4H, $2 \text{ OCH}_2\text{CH}_2$); $^{13}\text{C NMR}$ δ 71.9 (CH₂CH₂OC), 71.1 (CCH₂O(CH₂)₂N), 69.5 (CCH₂O octyl), 65.1 (OCH₂CH₂N), 57.8 (NCH₂CH₃), 54.4 (NCH₂CH₃), 45.3 (q C), 31.9 (CH₂CH₂CH₃), 29.7, 29.6, 29.4 (octyl CH₂), 26.3 (CH₂CH₂CH₂O), 22.7 (CH₂CH₃), 14.2 (Me), 8.4 (CH₂CH₃); HR ESI MS m/z calcd for C₃₇H₈₀N₂O₄/2 (M – 2Br)/2 308.3054, found 308.3038.

5,5-Bis(dodecyloxymethyl)-*N,N'*-diethyl-*N,N,N',N'*-dimethyl-3,7-dioxa-1,9-nonanediammonium dibromide (4.25). Ethyl bromide (2.3 mL, 31 mmol, 10 equiv) then sodium bicarbonate (1.30 g, 15.5 mmol, 5.0 equiv) were added to a stirred solution of compound **4.3** (2.13 g, 3.10 mmol) in THF (30 mL) and the resulting mixture was refluxed for 12 h, cooled to rt, and filtered, then the filtrate was concentrated to give the title compound as a colorless solid. Crystallization from ethyl acetate and acetone gave colorless granules: yield 2.37 g, 91.1%; mp 185 °C; R_f on basic alumina 0.45 (butanol:water:methanol 20:5:2); $^1\text{H NMR}$ δ 0.88 ppm (t, 6H, $J = 6.9$ Hz, $2 \times \text{Me}$), 1.27–1.31 (br s, 36H, $18 \times \text{CH}_2$), 1.45 (t, $J = 7.2$ Hz, 6H, $2 \times \text{NCH}_2\text{CH}_3$) 1.51 (pentet, 4H, $J = 6.2$ Hz, $2 \text{ OCH}_2\text{CH}_2$), 3.28 (s, 4H, dodecyl OCH₂C), 3.32 (t, $J = 6.6$ Hz, 4H, dodecyl OCH₂), 3.43 (s, 12H, $2 \times \text{N}(\text{CH}_3)_2$), 3.47 (s, 4H, CCH₂O(CH₂)₂N), 3.81 (q, 4H, $J = 7.3$ Hz, $2 \times \text{N}(\text{CH}_2\text{CH}_3)_2$), 3.92 (AA' part of AA'BB' pattern, 4H, $2 \text{ OCH}_2\text{CH}_2\text{N}$), 3.97 (BB' part of AA'BB' pattern, 4H, $2 \text{ NCH}_2\text{CH}_2\text{O}$); $^{13}\text{C NMR}$ δ 71.8 (CH₂CH₂OC), 70.9 (CCH₂O(CH₂)₂N), 69.4 (CCH₂Ododecyl), 65.3 (OCH₂CH₂N), 63.1 (NCH₂CH₂O), 61.0 (NCH₂CH₃), 51.3 (N(CH₃)₂), 45.1 (q C), 31.9 (CH₂CH₂CH₃), 29.7, 29.7, 29.5, 29.4 (dodecyl CH₂), 26.3 (CH₂CH₂CH₂O), 22.7 (CH₂CH₃), 14.2 (Me), 8.9 (NCH₂CH₃); HR ESI MS m/z calcd for C₄₁H₈₈BrN₂O₄ (M – Br) 751.5927, found 751.5922.

5,5-Bis(dodecyloxymethyl)-*N,N,N',N'*-dimethyl-3,7-dioxa-*N,N'*-dipropyl-1,9-nonanediammonium Dibromide (4.26). 1-Bromopropane (5.4 mL, 59 mmol, 10 equiv) then sodium bicarbonate (2.47 g, 29.4 mmol, 5.0 equiv) were added to a stirred solution of compound **4.3** (4.05 g, 5.89 mmol) in THF (50 mL) and the resulting mixture was refluxed for 26 h, cooled to rt, and filtered, then the filtrate was concentrated to give the title compound as a colorless solid. Crystallization from ethyl acetate and acetone gave colorless crystals: yield 4.83 g, 95.5%; mp 62 °C; R_f on basic alumina 0.50 (butanol:water:methanol 20:5:2); $^1\text{H NMR}$ δ 0.88 ppm (t, 6H, $J = 6.7$ Hz, $2 \times \text{Me}$), 1.05 (t, $J = 7.3$ Hz, 6H, $2 \times \text{N}(\text{CH}_2)_2\text{CH}_3$) 1.26–1.31 (br s, 36H, $18 \times \text{CH}_2$), 1.51 (pentet, 4H, $J = 6.2$ Hz, $2 \text{ OCH}_2\text{CH}_2$), 1.86 (AA' part of AA'XX' pattern, 4H, $2 \times \text{NCH}_2\text{CH}_2\text{CH}_3$), 3.28 (s, 4H, dodecylOCH₂C), 3.32 (t, $J = 6.6$ Hz, 4H, dodecyl OCH₂), 3.44 (s, 12H, $2 \times \text{N}(\text{CH}_3)_2$), 3.48 (s, 4H, CCH₂O(CH₂)₂N), 3.63

(XX' part of AA'XX' pattern 4H, 2 × NCH₂CH₂CH₃), 3.93 (AA' part of AA'BB' pattern, 4H, 2, OCH₂CH₂N), 3.99 (BB' part of AA'BB' pattern, 4H, 2, NCH₂CH₂O); ¹³C NMR δ 71.8 (CH₂CH₂OC), 70.9 (CCH₂O(CH₂)₂N), 69.5 (CCH₂O dodecyl), 67.1 (NCH₂CH₂CH₃), 65.4 (OCH₂CH₂N), 63.6 (NCH₂CH₂O), 51.9 (N(CH₃)₂), 45.2 (q C), 31.9 (CH₂CH₂CH₃), 29.7, 29.7, 29.5, 29.4 (dodecyl CH₂), 26.2 (CH₂CH₂CH₂O), 22.7 (CH₂CH₃), 16.5 (NCH₂CH₂CH₃), 14.2 (Me), 10.8 (N(CH₂)₂CH₃); HR ESI MS *m/z* calcd for C₄₃H₉₂BrN₂O₄ (M - Br) 779.6235, found 779.6209.

***N,N,N',N'*-Dibutyl-5,5-bis(dodecyloxymethyl)-*N,N,N',N'*-dimethyl-3,7-dioxo-1,9-nonanediammonium Dibromide (4.27).** 1-Bromobutane (4.70 mL, 44.0 mmol, 10 equiv) then sodium bicarbonate (1.84 g, 22.0 mmol, 5.0 equiv) were added to a stirred solution of compound **4.3** (3.03 g, 4.4 mmol) in THF (40 mL) and the resulting mixture was refluxed for 33 h, cooled to rt, and filtered, then the filtrate was concentrated to give the title compound as a colorless solid. Crystallization from ethyl acetate and methanol gave colorless crystals: yield 3.46 g, 88.7%; mp 110 °C; *R_f* on basic alumina 0.53 (butanol:water:methanol 20:5:2); ¹H NMR δ 0.88 ppm (t, 6H, *J* = 6.9 Hz, 2 × Me), 1.01 (t, *J* = 7.3 Hz, 6H, 2 × N(CH₂)₃CH₃), 1.26–1.31 (br s, 36H, 18 × CH₂), 1.48 (sextet, 4H, *J* = 7.4 Hz, 2 × NCH₂CH₂CH₂CH₃), 1.51 (pentet, 4H, *J* = 6.2 Hz, 2 OCH₂CH₂), 1.78 (AA' part of AA'XX' pattern, 4H, 2 × NCH₂CH₂CH₂CH₃), 3.28 (s, 4H, dodecylOCH₂C), 3.32 (t, *J* = 6.6 Hz, 4H, dodecyl OCH₂), 3.35 (s, 4H, N(CH₂)₂OCH₂C), 3.44 (s, 12H, 2 × N(CH₃)₂), 3.48 (s, 4H, CCH₂O(CH₂)₂N), 3.65 (XX' part of AA'XX' pattern, 4H, 2 × NCH₂CH₂CH₂CH₃), 3.94 (AA' part of AA'BB' pattern, 4H, 2 OCH₂CH₂N), 3.99 (BB' part of AA'BB' pattern, 4H, 2 NCH₂CH₂O); ¹³C NMR δ 71.9 (CH₂CH₂OC), 71.0 (CCH₂O(CH₂)₂N), 69.5 (CCH₂O dodecyl), 65.6 (NCH₂CH₂CH₂CH₃), 65.4 (OCH₂CH₂N), 63.7 (NCH₂CH₂O), 51.8 (N(CH₃)₂), 45.2 (q C), 32.0 (CH₂CH₂CH₃), 29.8, 29.7, 29.6, 29.4 (dodecyl CH₂), 26.3 (CH₂CH₂CH₂O), 24.9 (NCH₂CH₂CH₂CH₃), 22.7 (CH₂CH₃), 14.2 (Me), 13.9 (N(CH₃)₃CH₃); HR ESI MS *m/z* calcd for C₄₅H₉₆BrN₂O₄ (M - Br) 807.6553, found 807.6548.

***N,N,N',N'*-Tetramethyl-6,6-bis(octyloxymethyl)-4,8-dioxo-1,11-undecanediamine (5.1).** Sodium hydride (1.33 g, 55.4 mmol) was added slowly to a stirred solution of 2,2-dioctyloxymethyl-1,3-propanediol (**9**) (2.0 g, 5.5 mmol) in DMF (100 mL) under an N₂ atmosphere at 50 °C. The mixture was then stirred at 80 °C for 1 h. After the reaction mixture had been allowed to cool to rt, 3-chloro-*N,N*-dimethyl-1-propanamine hydrochloride (1.93 g, 12.2 mmol) was added in portions and the reaction mixture was stirred at 80 °C under nitrogen for another 24 h, then quenched with methanol and filtered. The filtrate was concentrated, and the residue was taken up in ethyl acetate (50 mL). This solution was washed with water (2 × 20 mL) and brine (20 mL), then dried (Na₂SO₄) and concentrated to a residue that was purified by flash column chromatography. Elution with a gradient of 10% to 15% methanol in dichloromethane gave compound **5.1** as a light brown liquid: yield 1.6 g (54%); *R_f* on basic alumina 0.6 (dichloromethane:methanol 93:7); ¹H NMR (CDCl₃) δ 0.88 (t, 6H, *J* = 6.5 Hz, 2 CH₃), 1.26–1.35 (m, 20H, 10 × CH₂), 1.52 (p, 4H, *J* = 7.0 Hz, 2 OCH₂CH₂), 1.71 (p, 4H, *J* = 6.5 Hz, 2 NCH₂CH₂), 2.22 (s, 12H, 2 N(CH₃)₂), 2.32 (t, 4H, *J* = 7.5 Hz, 2 NCH₂), 3.34 (t, 4H, *J* = 6.5 Hz, 2 CH₂CH₂O), 3.35 (s, 4H, 2 OCH₂), 3.37 (s, 4H, 2 OCH₂), 3.41 (t, 4H, *J* = 6.5 Hz, OCH₂); ¹³C NMR (CDCl₃) δ 71.7 (octyl CH₂O), 70.0 (OCH₂CH₂CH₂N), 69.85 (OCH₂C), 69.78 (OCH₂C), 57.0 (NCH₂), 45.64 (N(CH₃)₂), 45.59 (qC), 32.0 (CH₃CH₂CH₂), 29.82, 29.63, 29.49 (3 octyl CH₂), 28.2 (NCH₂CH₃), 26.4 (OCH₂CH₂CH₂), 22.9 (CH₃CH₂), 14.2 (CH₃); HR ESI MS *m/z* calcd for C₃₁H₆₇N₂O₄ (M + H) 531.5095, found 531.5087.

***N,N,N',N',N',N'*-Hexamethyl-6,6-bis(octyloxymethyl)-4,8-dioxo-1,11-undecanediammonium Diiodide (5.5).** Methyl iodide

(1.6 g, 11 mmol) was added to a stirred solution of amine **5.1** (0.6 g, 1.1 mmol) in THF (50 mL) and the reaction mixture was stirred for 36 h, then allowed to cool to rt. The reaction mixture was concentrated and the residue was purified by flash chromatography by using as eluant a gradient of 10% to 15% methanol in dichloromethane to give the title salt as an off-white solid: yield 0.7 g (68%); mp 212–215 °C; *R_f* 0.4 on basic alumina (8% methanol in dichloromethane); ¹H NMR (DMSO-*d*₆) δ 0.88 (t, 6H, *J* = 6.5 Hz, CH₃), 1.25–1.37 (m, 20 H, 10 × CH₂), 1.49 (p, 4H, *J* = 6.5 Hz, OCH₂CH₂), 1.96 (4H, AA' part of AA'BB' pattern, NCH₂CH₂), 3.11 (s, 18H, N(CH₃)₃), 3.31 (s, 4H, octylOCH₂C), 3.33 (t, 4H, *J* = 6.5 Hz, OCH₂), 3.36 (s, 4H, CH₂OCH₂C), 3.38 (4H, BB' part of AA'BB' pattern, NCH₂), 3.42 (t, 4H, *J* = 6.0 Hz, OCH₂); ¹³C NMR (CDCl₃) δ 70.7 (octyl CH₂O), 69.4 (OCH₂CH₂CH₂N), 68.8 (OCH₂C), 67.7 (OCH₂C), 63.3 (NCH₂), 52.3 (N(CH₃)₃), 45.0 (qC), 31.1 (OCH₂CH₂), 28.74, 28.65, 25.63 (decyl CH₂), 23.0 (NCH₂CH₂), 22.0 (CH₃CH₃), 13.9 (CH₃); HR ESI MS *m/z* calcd for C₃₃H₇₂IN₂O₄ (M - I), 687.4531; found, 687.4522.

Diethyl 3,13-Diazonia-3,3,13,13-tetramethyl-8,8-bis(octyloxymethyl)-6,10-dioxapentadecanedioate Dibromide (6.1). When a solution of compound **4.1** (0.61 g, 1.21 mmol) and ethyl bromoacetate (0.31 mL, 2.79 mmol, 2.3 equiv) in diethyl ether (20 mL) was stirred for 26 h, a colorless solid formed that was isolated by filtration, then washed with ether. The solid was crystallized from ethyl acetate and methanol to give the title compound as a colorless crystalline solid: yield 0.88 g, 84%; mp 110–111 °C; *R_f* on basic alumina 0.59 (butanol:water:methanol 20:5:2); ¹H NMR δ 0.88 (t, 6H, *J* = 6.9 Hz, 2 × Me), 1.27 (br s, 20H, 10 × CH₂), 1.32 (t, 6H, *J* = 7.2 Hz, 2 × Me), 1.50 (pentet, 4H, *J* = 6.0 Hz, 2 OCH₂CH₂), 3.28 (s, 4H, octyl OCH₂C), 3.33 (t, 4H, *J* = 6.6 Hz, octyl OCH₂C), 3.50 (s, 4H, CCH₂O(CH₂)₂N), 3.71 (s, 12H, 2N(CH₃)₂), 3.96 (br AA' part of AA'BB' pattern, 4H, 2 OCH₂CH₂N), 4.27 (q, 4H, *J* = 7.2 Hz, OCH₂CH₃), 4.32 (br BB' part of AA'BB' pattern, 4H, 2 NCH₂CH₂O), 4.96 (s, 4H, CH₂COOR); ¹³C NMR δ 164.9 (CH₂COOR), 71.8 (CH₂CH₂OC), 71.1 (CCH₂O(CH₂)₂N), 69.4 (CCH₂O octyl), 65.4 (OCH₂CH₂N), 64.1 (NCH₂CH₂O), 62.7 (CH₂COOCH₂CH₃), 62.3 (CH₂COOCH₂CH₃), 52.4 (N(CH₃)₂), 45.1 (qC), 32.0 (CH₂CH₂CH₃), 29.6, 29.5, 29.3 (octyl CH₂), 26.2 (CH₂CH₂CH₂O), 22.7 (CH₂CH₃), 14.12 (Me), 14.06 (CH₃CH₂); HR ESI MS *m/z* calcd for C₃₇H₇₆N₂O₈/2 ((M - 2Br)/2) 338.2795, found 338.2811.

3,13-Diazonia-3,3,13,13-tetramethyl-8,8-bis(octyloxymethyl)-6,10-dioxapentadecanedioate (6.5). Compound **6.1** (0.44 g, 0.51 mmol) and IRA-400 anion-exchange resin (OH⁻) (11.0 g) in ethanol (30 mL) were stirred at rt for 24 h. The reaction mixture was filtered and the filtrate was concentrated to a semisolid residue that precipitated from ethyl acetate and methanol to give the title compound as a colorless waxy mass: yield 0.28 g, 90%; mp 183 °C; *R_f* on basic alumina 0.37 (butanol:water:methanol 20:5:2); ¹H NMR δ 0.88 (t, 6H, *J* = 6.7 Hz, 2 × Me), 1.28–1.32 (br s, 20H, 10 × CH₂), 1.51 (pentet, 4H, *J* = 6.2 Hz, 2 OCH₂CH₂), 3.29 (s, 4H, octyl OCH₂C), 3.33 (t, 4H, *J* = 6.4 Hz, octyl OCH₂), 3.39 (s, 4H, CCH₂O(CH₂)₂N), 3.39 (s, 12H, 2N(CH₃)₂), 3.82 (br AA' part of AA'BB' pattern, 4H, 2 NCH₂CH₂O), 3.99 (BB' part of AA'BB' pattern, 4H, 2 OCH₂CH₂N), 3.99 (s, 4H, CH₂COO⁻); ¹³C NMR δ 166.2 (CH₂COO⁻), 71.4 (CH₂CH₂OC), 70.6 (CCH₂O(CH₂)₂N), 69.2 (CCH₂O octyl), 65.46 (NCH₂CH₂O), 65.3 (OCH₂CH₂N), 62.4 (CH₂COO⁻), 52.0 (N(CH₃)₂), 44.7 (q C), 31.6 (CH₂CH₂CH₃), 29.3, 29.2, 29.1 (octyl CH₂), 25.9 (CH₂CH₂CH₂O), 22.4 (CH₂CH₃), 13.8 (Me); HR ESI MS *m/z* calcd for C₃₃H₆₇N₂O₈ (M + H) 619.4892, found 619.4859.

Acknowledgment. We thank the Atlantic Innovation Fund and the Natural Sciences and Engineering Research

Council (NSERC) of Canada for support. Christian Petropolis is grateful for an NSERC USRA award. NMR spectra were recorded at the Atlantic Region Magnetic Resonance Centre. We thank Eric Bond, Malcolm Huestis, Douglas Staple, and Tyler Mercer for preparation of starting materials and Dr. Eugen A. Karpichev and Tyler Mercer for measurement of surface tensions. We are also grateful to

Dr. Hussein Al-Mughaid for performing some preliminary experiments.

Supporting Information Available: Experimental procedures, characterization data, and ^1H NMR and ^{13}C NMR spectra of all new compounds. This material is available free of charge via the Internet at <http://pubs.acs.org>.