**Headgroup Effects on the Kraft Temperatures and Self-assembly of ω-Hydroxy and ω-Carboxy Hexadecyl Quaternary Ammonium Bromide Bolaform Amphiphiles: Micelles versus Molecular Clusters?**

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**ABSTRACT**

Eight bolaform amphiphiles were synthesized and characterised; 4 ,-hydroxy-alkane trialkyl (and pyridyl) ammonium bromides and 4 ,-carboxy-alkane trialkyl (and pyridyl) ammonium bromides where the alkyl groups were methyl, ethyl and propyl. 4 of these represented new compounds. Overall the Krafft temperatures (TK) of the eight amphiphiles were high, with 6 of the 8 possessing TKs greater than 45ºC. Thus most of the amphiphiles could only expect to find applications at raised temperatures limiting their potential utility. However in addition to the previously reported ,-hydroxy-hexadecyl triethylammonium bromide (**2b**) with a TK of 19.1°C, another amphiphile, ,-carboxy-hexadecyl tripropylammonium bromide (**2c**) has been identified with a TK near ambient temperatures (TK of 22.1°C). This provides an acid functional ammonium bolaform amphiphile that micellises at ambient tempratures to complement the hydroxyl derivative. A correlation between TK and the product of the enthalpies and Tms of the compounds was observed for 7 of the 8 compounds. No correlation between the amphiphile critical micelle concentrations (cmc) and TKs was observed confirming previous reports that TK values are predominantly determined by crystalline stability rather than solubility. Considerable differences were observed between the various amphiphile TKs at different pHs but no clear trend was apparent for the various compounds (despite the degree to which the compounds’ carboxylic acid and hydroxyl functionalities were likely to be ionized). The cmcs for the amphiphiles were an order of magnitude larger than those for analogous mono-ammonium amphiphiles with little difference in between the hydroxyl- and carboxy-functionalised compounds. The aggregation numbers (Nagg) obtained for all compounds were very low (Nagg<7) and the apparent micellar diameters for the hydroxyl-bolaforms were in the range 1.0 to 1.4 nm whereas those for the carboxy-compounds were in the range 2.1 to 2.4 nm. These results strongly suggest a difference in the packing of the two sets of amphiphiles with loose low density aggregates or ‘molecular clusters’ for the carboxy compounds and more dense classical micellar type aggregates for the hydroxyl-compounds. In both cases however the sizes and the low aggregation numbers point suggest that these aggregates are more characteristic of the pre-micellar aggregates observed for many amphiphiles but in particular gemini surfactants.

*Keywords:* Micelle; aggregate; pre-micellar; ammonium; bolaform; amphiphile; self-assembly; dynamic light scattering; Krafft temperature; aggregation number.

**1. Introduction**

Most typically the simplest and most commonly used, general purpose surfactants possess a hydrophobic region (non-polar) which is a long alkyl chain and a hydrophilic region (polar) region usually positively or negatively charged in water. In recent times, an increasing number of surfactants with more complicated structures have been developed including gemini, fluorinated, siloxane and bolaform surfactants.[1] Bolaform surfactants are α,ω-dipolar molecules that possess two or more hydrophilic groups separated by a hydrophobic region and were first described by Fuoss & Edelson, 1951.[2, 3] They can be considered as two conventional amphiphiles that are covalently linked through their hydrophobic chain ends and the simplest and most studied of these are the symmetrical alkane-bis(trialkyl ammonium halide) salts,[4-15] which are bolaform analogues of the alkane trialkylammonium salts such as cetyl trimethyl ammonium bromide (CTAB). Differences between simple bolaform amphiphiles and the simple mono-amphiphiles (with one headgroup per chain) include their higher critical micelle concentrations (cmc) and the formation of smaller micelles.[10, 12],[16-18] The former can be rationalised by the increased hydrophilic-hydrophobic balance of the molecule and the latter by consideration of the packing of the chain in a micelle, which whether extended or ‘bent’, would lead to micelles with diameters approximately half those of conventional surfactants with equivalent hydrophobic chain lengths (Figure 1).

Bolaform vs CTAB micelle last.tif

**Figure 1.** Idealised schematic illustration of difference in size between standard micelle from mono-functional alkyl compound and a bolaform amphiphile.

Increasing interest has been paid to non-symmetrical ,-bolaform amphiphiles which possess two different headgroups and that consequently might be expected to present both functional groups at the surface of any aggregates, micellar or otherwise.[19, 20] Hayman *et al.* described the synthesis of a number bolaform amphiphiles including some ,-hydroxy-alkane trialkylammonium bromides and a single ,-carboxy-alkane trialkylammonium bromide and further reported on the Krafft temperatures (TK) and aggregation properties of the molecules.[21-23] As well as showing promising anti-microbial properties one of these compounds, N,N,N-triethyl-16-hydroxyhexadecan-1-ammonium bromide, proved useful in standard silicate templating reactions resulting in highly ordered silicate materials being produced with pore sizes between diameters of 1.0 to 2.0 nm (termed super-microporous silicates).[24-26] This was postulated to be as a consequence of the formation of micelles with diameters approximately 50% the size of those of standard CTAB-type templates used in the synthesis of mesoporous silicate materials (typical pore sizes > 3.0 nm). No further reports of the use of bolaform amphiphiles as silicate templating agents have appeared.

The ultimate aim of this work was to utilise bolaform amphiphiles in the templating of supermicroporous silicates with defined porosity that would be controlled by the structure and chemistry of the template surfactants. Thus this paper describes the synthesis and characterisation of a range of bolaform amphiphiles (including some previously reported on by Hayman *et al*);. 4 new and 4 previously synthesised ω-hydroxy and ω-carboxy hexadecyl quaternary ammnium bromide bolaform amphiphiles, with trimethyl-, triethyl-, tripropyl- and pyridyl ammonium headgroups. In order to understand any relationships between templating activity and self-assembly a number of physical properties of the the bolaform ammonium surfactant solutions needed to be determined: (i) TK values (ii) cmcs; (iii) aggregate sizes; (iv) aggregation numbers. This would enable a direct comparison of the effect of the hydroxyl headgroups compared to carboxylic acid headgroups, with systematic variation of the structure of the ammonium headgroups, on these values and importantly on their self-assembly in solution. To date there have been no aggregate size measurements of the hydroxyl- or carboxy- ammonium amphiphiles and no data on the effect of pH on their TK values. This paper describes the results of this study.

**2. Experimental Section**

*2.1 Materials*

Trimethylamine (33%, in ethanol), triethylamine (99%), tripropylamine (98%), pyridine (99+%, anhydrous), borane-methyl sulfide complex, hydrobromic acid (48%), ammonium hydroxide (28-30%) and ethyl acetate (99.8%) were purchased from Aldrich. Sulfuric acid (H2SO4) (98%), dichloromethane (DCM) (99.99%, analytical grade), sodium chloride, water (analytical grade), magnesium sulfate (MgSO4) (99%), toluene (99%, analytical grade), ethanol (99.99%, analytical grade), acetonitrile (99.98%, analytical grade), acetone (99%, analytical grade), sodium hydroxide, diethyl ether (99%, analytical grade), hydrochloric acid (37%), hexane (99%, analytical grade), methanol (99%, analytical grade), chloroform (99.99%, analytical grade), water (HPLC grade), hydrochloric acid (37%, laboratory grade) and sodium bicarbonate (99%) were all purchased from Fisher. Potassium hydroxide, potassium hydrogen carbonate, cetyl trimethyl ammonium bromide, tetramethyl ammonium hydroxide and sodium silicate was purchased from BDH Laboratory Supplies. Hexadecan-16-olide was purchased from Fleurchem Inc. Di-isopropyl ether was purchased from Riedel-de Haën. NMR solvents chloroform-d (99.8%), deuterium oxide (99.9%) and methanol-d (99.8%) were purchsed from GOSS Scientific Instruments Ltd. Tetrahydrofuran (THF) (99.5%, analytical grade, Fisher) was pre-dried over magnesium sulfate and sodium wire, then distilled over sodium wire and benzophenone immediately prior to use. Potassium chloride was purchased from Carlo Erba Reagents. Solid fumed silica Aerosil 200 was purchased from Degussa. Sodium hydroxide was ordered from Riedel-de Haën.

Tetraethyl ortho-silicate was ordered from Fluka Chemie. All reagents were used as received. The bolaform amphiphiles were all synthesised in the laboratory (as detailed earlier). All water was deionised using a Purite HP700 laboratory deioniser.

*2.2 Characterisation of Bolaform amphiphiles.*

All surfactants (**1a**-**1d** and **1a**-**2d**) were dried prior to analysis in an oven overnight at 60°C and cooled in a desiccator. They were then transferred to a sealed container and stored in a refrigerator.1H and 13C NMR spectra were recorded in 5mm NMR tubes using a JEOL GX-270FT at 270MHz at 30ºC with Me4Si and CDCl3 (centre line at *δ* 77.00 ppm relative to Me4Si) as internal standards. 1-2 drops of MeOH-d4 were also added to completely dissolve the sample. All NMR spectra were recorded at 27°C. Spectra were interpreted using SpecNMR version 1.0 computer software.Infra-red spectra were recorded using a Thermo Electron Corporation Nicolet 380 FTIR with a Smart Orbit Diamond ATR 30,000 to 200 cm-1 attachment; a small amount of the dry sample (around 0.2 g) was placed on the sample disc and analysed directly. Electro-spray mass (ES-MS) spectra were recorded with a Thermo Finnigan LCQ Classic where 1 ml of a 1:1 solution of methanol/water was added to a small amount of the sample (1 mg) in an Eppendorf tube and shaken till the sample dissolved. If the sample did not dissolve, the tube was placed in a sonicator water bath for 5 to 10 minutes at room temperature. The solution was then diluted 1:10 ratio using using a mixture of 1:1 solution of methanol/water. Results were collected using LCQ tune software. Elemental [CHN] analysis was recorded by combustion with a Carlo Erba 1106 where an accurately weighed amount of the dry sample (1.2 to 1.4 mg) was sealed in a small tin capsule and combusted at 1020°C. The thermal behaviour of the amphiphiles was investigated using a Perkin Elmer differential scanning calorimeter (PE DSC 7) calibrated against the melting point of Indium (mp = 156.1°C, ΔH = 28.3 J/g). In all cases, 30 μL aluminium crimped pans were used. The baseline was corrected by using 2 empty aluminium crimped pans and the sample was prepared by crimping 10-20 mg of the sample.

*2.3 Syntheses*

*16-bromohexadecanoic acid.*16-Bromohexadecanoic acid was synthesised using the method published by Chuit and Hausserfor the synthesis of 15-bromopentadecanoic acid.[27] Hexadecan-16-olide (24 g, 50 mmol) was added to concentrated HBr (56 ml) and sulfuric acid (15 ml) in a 100 ml round-bottomed flask and heated under reflux for 31/2 days afterwards. The reaction mixture was dissolved in hot dichloromethane (400 ml), filtered, washed with saturated sodium chloride solution (200 ml), water (200 ml), dried over MgSO4 and concentrated under vacuum to give the crude product. This material was then recrystallised from acetonitrile and filtered to yield 30.1 g (95%) of **1**: 1H NMR *δ* 3.41 ppm (t, 3H, BrC*H*2), 2.35 ppm (t, 3H, HO2CC*H*2), 1.85 ppm (m, 5H, BrCH2C*H*2), 1.63 ppm (m, 5H, HO2CCH2C*H*2), 1.13 – 1.49 ppm (m + s at 1.26 ppm, 22 H, BrCH2CH2(C*H*2)11). 13C NMR *δ*  179.44 (C=O); 34.18, 34.05, 33.01, 29.75, 29.59, 29.39, 29.20, 28.93, 28.33, 24.83 (CH2). Anal. Cald for C16H31O2Br: C, 57.30; H, 9.54. Found: C, 57.85; H, 9.56. IR 1693.5 cm-1 (C=O), 715.7 cm-1 (C-Br), 2913.6 cm-1 and 2848.8 cm-1 (C-H).

*16-bromohexadecan-1-ol.*16-Bromohexadecan-1-olwas prepared by borane reduction of the corresponding bromo-acid according to the method published by De Vries *et al.[28]* Borane (2.66 g, 35 mmol) in THF (35 ml) was added drop wise to a stirring solution of 16-Bromohexadecanoic acid (8.11 g, 24 mmol) in THF (70 ml) and stirred for 1 hour at ambient temperature after which he solution was diluted with 1 M NaOH and extracted with diethyl ether. This extract was washed with 1 M HCl, dried and evaporated and the residue crystallised from hexane to yield 5.5 g (72%) of **3**: 1H NMR *δ* 3.64 ppm (t, 3H, BrC*H*2), 3.41 ppm (t, 3H, BrC*H*2) 1.86 ppm (m, 5H, BrCH2C*H*2), 1.57ppm (m, 5H, HOCH2C*H*2), 1.11 – 1.47 ppm (m + s at 1.26 ppm, 22H, BrCH2CH2(C*H*2)11). 13C NMR *δ* 63.27 (C-O); 34.21, 33.02, 32.98, 29.80, 29.77, 29.59, 28.33, 25.89 (CH2)*.* Anal. Cald for C16H33OBr: C, 59.80; H, 10.35. Found: C, 59.80; H, 10.47.IR 3266.8 cm-1 (O-H), 719.0 cm-1 (C-Br), 2915.2 cm-1 and 2847.0 cm-1 (C-H).

*15-carboxy-N,N,N-trimethylpentadecan-1-ammonium bromide (****1a****), 15-carboxy-N,N,N-triethylpentadecan-1-ammonium bromide (****1b****) and 1-(15-carboxypentadecyl)pyridinium bromide (****1d****).*The 15-carboxy-N,N,N-trialkylpentadecan-1-ammonium bromides (**1a**, **1b** and **1d**)were all synthesised following the method published by Hayman *et al.[23]* for the previous synthesis of **1a** whereby a mixture of 6.0 g (0.3 mmol) of 16-bromohexadecanoic acid was combined with 10 molar equivalents of trimethylamine and heated at 80ºC in a sealed tube for 4 days. The reaction mixture was then filtered and the solid obtained was recrystallised from ethanol to yield 3.5 g (63%) of **1a**: mp (DSC) 233.6°C. 1H NMR *δ* 3.36 ppm (t, 2H, (CH3)3N+C*H*2), 3.19 ppm (s, 9H, (C*H*3)3N+CH2), 2.29 ppm (t, 2H, HO2CC*H*2), 1.76 ppm (m, 2H, (CH3)3N+CH2C*H*2), 1.61 ppm (m, 2H, HO2CCH2C*H*2), 1.12 - 1.45 ppm (m + s at 1.27 ppm 22H, HO2CCH2CH2(C*H*2)11). 13C NMR *δ*  176.96 (C=O); 67.59 (C-O); 53.52 (C-N); 34.53, 29.84, 29.75, 29.67, 29.58, 29.49, 29.44, 26.57, 25.33, 23.41 (CH2). Anal. Cald for C19H40BrNO2: C, 57.85; H, 10.22. Found: C, 58.97; H, 10.55. IR 1693.6 cm-1 (C=O), 2913.6 cm-1 and **2847.7 cm-1 (C-H). ESMS: 314.4 m/z.**

Identical procedures were followed for the syntheses of **1b** and **1d**. The reaction conditions and product yields are given in Table 1.

**1b**: mp (DSC) 77.0°C. 1H NMR *δ* 4.07 ppm (t, 2H, (CH3 CH2)3N+C*H*2), 3.64 ppm (m, 6H, (CH3C*H*2)3N+CH2), 2.32 ppm (t, 2H, HO2CC*H*2), 1.63 ppm (m, 4H, (N+CH2C*H*2(C*H*2)11C*H*2), 1.12 - 1.45 ppm (m + t at 1.21 ppm 31H, (C*H*2)11CH2N+(CH2C*H*3)3). 13C NMR *δ*  174.35 (C=O); 64.59 (C-O); 58.13 (C-N); 34.54, 29.73, 29.67, 29.61, 29.56, 29.35, 29.26, 28.77, 26.03, 25.13, 18.20 (CH2). IR 1725.2 cm-1 (C=O), 3350.0 cm-1 (O-H), 2915.9 cm-1 and 2848.5 cm-1 (C-H). Anal. Cald for C22H46BrNO2: C, 60.53; H, 10.62. Found: C, 70.60; H, 11.62.

**1d:** mp (DSC) 180.0°C­. 1H NMR *δ* 9.03 ppm (d, 1H, (*ortho* pyridyl), 8.57 ppm (t, 1H, (*para* pyridyl), 8.14 ppm (t, 1H, *meta* pyridyl), 4.70 ppm (t, 2H, (N+C*H*2CH2), 2.29 ppm (t, 2H, HO2CC*H*2), 2.04 ppm (m, 2H, N+CH2C*H*2), 1.61 ppm (m, 2H, HO2CCH2C*H2*), 1.12 - 1.45 ppm (m + s at 1.27 ppm, 22H, HO2CCH2CH2(C*H*2)11); 13C NMR *δ*  176.85 (C=O); 145.79, 144.91, 128.85 (pyridyl); 62.67 (C-O); 34.44, 31.87, 29.75, 29.65, 29.53, 29.49, 29.39, 29.21, 26.34, 25.22 (CH2). IR 1720.0 cm-1 (C=O), 3413.4 cm-1 (O-H), 2917.96 cm-1 and 2849.2 cm-1 (C-H). Anal. Cald for C21H36BrNO2: C, 60.86; H, 8.76. Found: C, 61.20; H, 9.05. ESMS: 334.3 m/z.

*15-carboxy-N,N,N-tripropylpentadecan-1-ammonium bromide (****1c****).*Difficulties were encountered following the procedure published by Hayman *et al.[23]*However, **1c** was successfully synthesised usinga3-step synthesis (protection, quaternisation and deprotection) following published procedures (see results and discussion) as follows.[29]

1. *Methyl 16-bromohexadecanoate.*A mixture of 16-bromohexadecanoic acid (1.407 g, 1.4 mmol), methanol (600 ml) and concentrated sulphuric acid (0.6 ml) was refluxed under nitrogen for 24 hours and then rotary evaporated. A solution of the residue in chloroform was washed twice with 5% sodium bicarbonate and then with water. The solution was then rotary evaporated to leave the crude product. This material was chromatographed on a 20 cm x 1.5 cm column of silica gel packed in hexane and eluted with 1:20 ethyl acetate-hexane to give the product. 1H NMR *δ* 3.64 ppm (s, 3H, C*H3*O2C), 3.38 ppm (t, 2H, BrC*H*2), 2.28 ppm (t, 2H, CH3O2CC*H*2), 1.83 ppm (m, 2H, BrCH2C*H2*), 1.59 ppm (m, 2H, O2CCH2C*H*2), 1.08 - 1.46 ppm (m + s at 1.23 ppm 22H, O2CCH2CH2(C*H*2)11).
2. *(15-(methoxycarbonyl)pentadecyl)trimethyl ammonium bromide.*A mixture of 16-bromohexadecanoate 1.23g, 35.1 mmol) and tripropylamine (6.6 ml) were heated in a sealed tube at 80ºC for 4 days. The reaction mixture was filtered and the solid obtained was recrystallised from a chloroform/hexane mixture. 1H NMR *δ* 3.36 ppm (m, 8H, (CH3CH2C*H2*)3N+C*H*2), 2.30 ppm (t, 2H, C*H2*COOCH3), 1.53 – 1.90 ppm (m, 10H, (CH3C*H2*CH*2*)3N+CH2C*H2*(CH2)11C*H2*), 1.15 – 1.46 ppm (m + s at 1.25 ppm, 22H, CH3O2CCH2CH2(C*H*2)11), 1.07 ppm (t, 9H, (C*H3*CH2CH2)3N+).
3. *15-carboxy-N,N,N-tripropylpentadecan-1-ammonium bromide (****1c****).*A mixture of (15-(methoxycarbonyl)pentadecyl)trimethyl ammonium bromide (3.21 g, 0. 59 mmol), potassium hydroxide (3.69 ml, 5.0 mmol), water (262.9 ml) and ethanol (262.9 ml) was refluxed for 2 days and rotary evaporated. Water (262.9 ml) was added to the residue and then the pH of the resultant solution was adjusted to 1 with concentrated hydrobromic acid to precipitate the crude product. This material was collected and washed with acetone and then chloroform to give the solid product. This solid product was then recrystallised from 1:1.5 methanol-diethyl ether.mp (DSC) 77.7 °C. ­1H NMR *δ* 3.61 ppm (t, 2H, C*H2*COOH), 3.33 ppm (m, 8H, (CH3CH2C*H2*)3N+C*H*2), 1.46 – 1.92 ppm (m, 8H, (CH3C*H2*CH*2*)3N+CH2C*H2*), 1.14 – 1.43 ppm (m + s at 1.22 ppm, 24H, (C*H*2)11C*H2*CH2COOH), 1.04 ppm (t, 9H, (C*H3*CH2CH2)3N+). 13C NMR *δ*  176.49 (C=O); 60.43 (C-O); 59.03 (C-N); 33.99, 29.40, 29.28, 29.11, 28.99, 26.26, 24.80, 21.89, 15.48, 10.44 (CH2). Anal. Cald for C25H52BrNO2: C, 62.74; H, 10.95. Found: C, 51.53; H, 9.22. IR 1731.5 cm-1 (C=O), 2968.3 cm-1, 2914.9 cm-1, 2873.3 cm-1 and 2846.3 cm-1 (C-H).

*16-hydroxy-N,N,N-trimethylhexadecan-1-ammonium bromide (****2a****) and 1-(16-hydroxyhexadecyl)pyridinium bromide (****2d****).* **2a** and **2d** were both synthesised using the method published by Hayman *et al.[23]* **2a** was synthesised whereby a mixture of 8.0 g (0.62 mmol) of 16-bromohexadecanol was combined with 10 molar equivalents of trimethylamine and heated at 80ºC in a sealed tube for 4 days. The reaction mixture was then filtered and the solid obtained recrystallised from water to yield 1.7 g (74%) of **2a**: mp (DSC) 212.3°C­­. 1H NMR *δ* 3.57 ppm (t, 3H, C*H2*OH), 3.20 ppm (s, 9H, (C*H*3)3N+CH2), 1.76 ppm (m, 2H, N+C*H2*), 1.55 ppm (m, 2H, (CH3)3N+CH2C*H*2), 1.15 – 1.45 ppm (m + s at 1.27 ppm 22H, HOCH2C*H2*(C*H*2)11). 13C NMR *δ*  67.39 (C-N); 62.62, 53.46 (C-O); 32.79, 29.82, 29.68, 29.56, 29.35, 26.43, 26.03, 23.31 (CH­2). IR 3345.7 cm-1 (O-H), 2915.7 cm-1 and 2847.9 cm-1 (C-H). Anal. Cald for C19H42BrNO: C, 59.98; H, 11.13. Found: C, 59.41; H, 11.11.

**2d** was synthesised whereby a mixture of 3.4 g (10.6 mmol) of 16-bromohexadecanoic acid was combined with 10 molar equivalents of pyridine and heated at 80ºC in a sealed tube for 13 hours. The reaction mixture was then filtered and the solid obtained was recrystallised from a mixture of methanol and water to yield 3.2 g (76%) of **2d**:mp (DSC) 150.5°C­­. 1H NMR *δ* 9.07 ppm (m, 1H, (*ortho* pyridyl), 8.56 ppm (m, 1H, (*para* pyridyl), 8.14 ppm (m, 1H, *meta* pyridyl), 4.71 ppm (t, 2H, (N+C*H*2CH2), 3.57 ppm (t, 2H, HOC*H*2), 2.04 ppm (m, 2H, N+CH2C*H*2), 1.00 - 1.68 ppm (m + s at 1.26 ppm, 26H, HOCH2C*H2*(C*H*2)12). 13C NMR *δ* 145.79, 144.91, 128.88 (pyridyl); 62.68 (C-O); 32.83, 31.87, 29.84, 29.70, 29.56, 29.24, 26.35, 26.06 (CH2). IR 3381.2 cm-1 (O-H), 2912.4 cm-1 and 2846.8 cm-1 (C-H). Anal. Cald for C19H38BrNO: C, 62.98; H, 9.57. Found: C, 58.56; H, 9.53.

*16-hydroxy-N,N,N-triethylhexadecan-1-ammonium bromide (****2b****) and 16-hydroxy-N,N,N-tripropylhexadecan-1-ammonium bromide (****2c****).* **2b** and **2c** were both synthesised following the method published by Hayman *et al.[23]***2b** was synthesised whereby a mixture of 3.5 g (10.9 mmol) of 16-bromohexadecanol was combined with 10 molar equivalents of triethylamine and heated under reflux in ethanol for 4 days. The reaction mixture was then filtered and the solid obtained was recrystallised from a mixtures of ethanol/diethyl ether and then ethanol/diiosopropyl ether to yield 1.9 g (42%) of **2b**: mp (DSC) 130.9°C­­. 1H NMR *δ* 3.64 ppm (m, 2H, C*H2*OH), 3.53 ppm (m, 6H, (CH3C*H*2)3N+), 3.27 ppm (m, 2H, (CH3CH2)3N+C*H2*), 1.50 – 1.77 ppm (m, 4H, C*H2*(CH2)12C*H2*), 1.15 – 1.45 ppm (m, 33H, (C*H*2)12CH2CH2N+(CH2C*H3*)3; IR 3268.1 cm-1 (O-H), 2914.9 cm-1 and 2848.2 cm-1 (C-H). Anal. Cald for C22H48BrNO: C, 62.53; H, 11.45. Found: C, 61.89; H, 11.94. 13C NMR *δ*  63.07 (C-N); 57.79, 53.77 (C-H); 46.25, 32.95, 29.62, 29.52, 29.48, 29.26, 26.62, 25.89, 22.27, 8.81, 8.27 (CH2).

**2c** was synthesised whereby a mixture of 1.5 g (5.9 mmol) of 16-bromohexadecanol was combined with 10 molar equivalents of tripropylamine and heated under reflux in ethanol for 5 days. The reaction mixture was then filtered and the solid obtained was recrystallised from a mixture of ethanol/diethyl ether and then ethanol/ethyl acetate to yield 1.5 g (70%) of **2c**: mp (DSC) 85.7 °C­­. 1H NMR *δ* 3.64 ppm (t, 2H, (C*H2*OH), 3.37 ppm (m, 9H, (CH3CH2C*H2*)3N+C*H*2), 1.50 – 1.88 ppm (m, 8H, (CH3C*H2*CH*2*)3N+CH2C*H2*), 1.14 – 1.45 ppm (m + s at 1.26 ppm, 26H, (C*H*2)12C*H2*CH2OH), 1.07 ppm (t, 9H, (C*H3*CH2CH2)3N+). 13C NMR *δ*  62.69 (C-N); 60.99, 59.54 (C-H); 32.86, 29.55, 29.42, 29.21, 26.51, 25.80, 22.44, 16.10, 11.00 (CH2). IR 3271.0 cm-1 (O-H), 2915.0 cm-1 and 2848.0 cm-1 (C-H). Anal. Cald for C25H54BrNO: C, 64.62; H, 11.72. Found: C, 64.20; H, 11.98.

*2.4 Krafft temperature determination (TK).*

The Krafft temperatures of the bolaform amphiphiles were determined at pH 2.2, 7.0 and 11.5. Samples were prepared for TK determination by dissolving **1a-d** and **2a-d** at 1% (w/v) in pH 2 buffer (0.0078 M HCl, 0.022 M KCl; *I* = 0.030), pH 7 buffer (de-ionised water) and pH 11.5 buffer (0.013 M KHCO3, 0.020 M KOH; *I* = 0.046). Each sample was heated in a water bath and the temperature at which the solid dissolved or precipitated out (on cooling) was recorded following published procedures.[22] Each measurement was performed three times and the average value was recorded.

*2.5 Critical micelle concentration (CMC) determination using 1H NMR spectroscopy.*

The CMCs of the bolaform amphiphiles were determined using 1H NMR chemical shifts following published procedures.6 To prepare the samples for 1H NMR analysis, 10 concentrations (0.5 g/L to 5.0 g/L) of each bolaform amphiphile species were prepared in deuterium oxide. Each sample was heated to above its Krafft temperature and then transferred to an NMR tube. Nuclear magnetic resonance (NMR) spectra were recorded on a JEOL GX-270FT spectrometer at 270MHz in D2O using an insert of dioxane as an external reference (3.700 ppm). In all cases, the measurements were performed 10°C above the Krafft temperature of the surfactant. The free induction decays (FIDs) were interpreted using SpecNMR version 1.0 computer software to generate the spectra.

*2.6 Micelle size determination using dynamic light scattering (DLS).*

1% (w/v) solutions of the samples was prepared in HPLC grade water and then transferred to a cuvette ready for analysis. DLS measurements were performed on the surfactant solutions using a Malvern Zetasizer Nano ZS using Dispersion Technology Software (DTS) version 5.0 software. All measurements were performed 10°C above the Krafft temperature of the surfactant and each measurement was repeated twice more and the average was recorded.

*2.7 Cryo-transmission electron microscopy (cryo-TEM).*

*Cryo*-TEM was performed at the Hebrew University of Jerusalem, Israel using a Tecnai F20 G2 microsope. 1% (w/v) solutions of surfactants **2a**, **2b** and **2d** were prepared in water and subsequently cooled very rapidly by injecting the solution into liquid ethane prior to analysis.

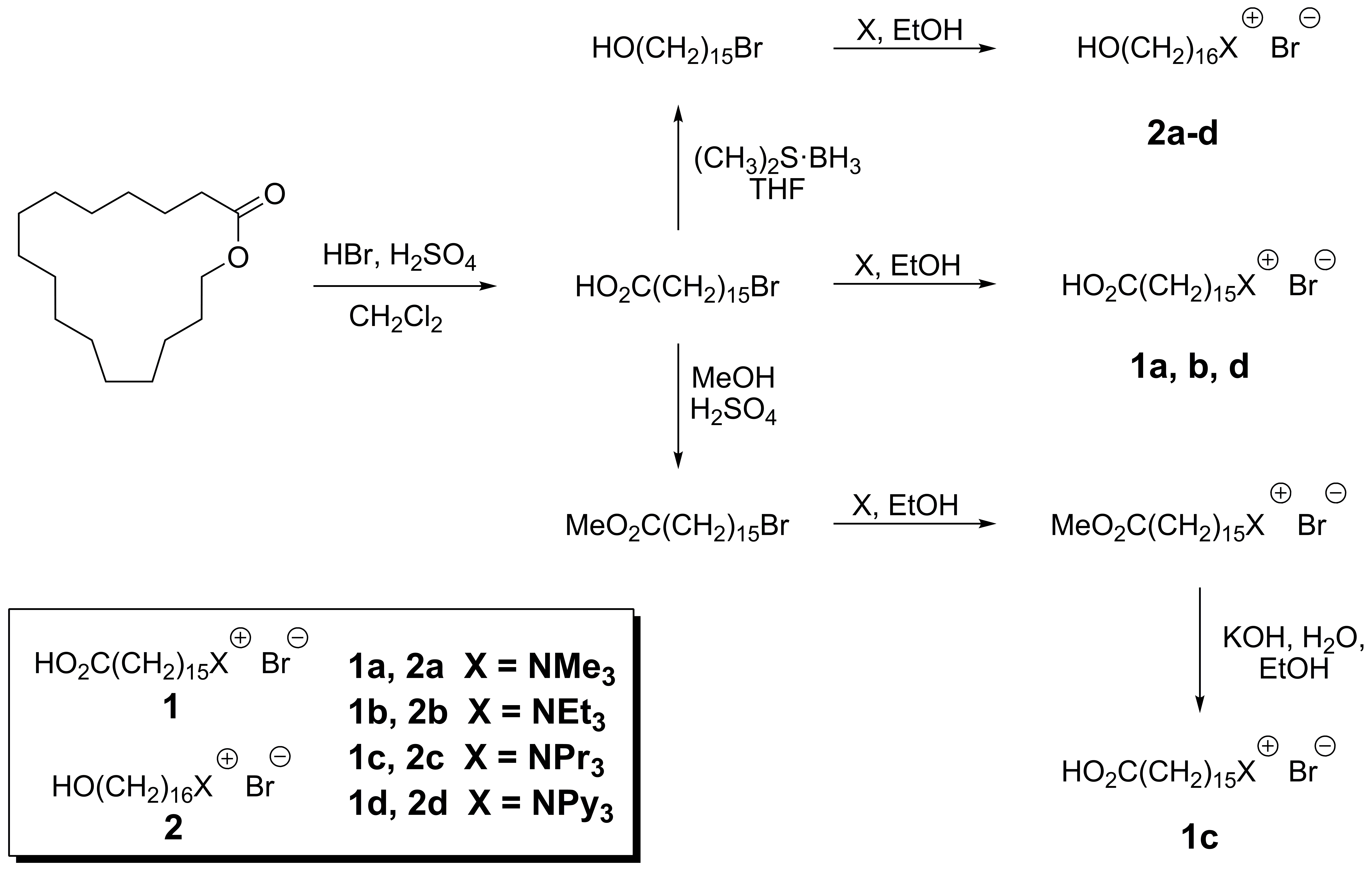
*2.8 Molecular Modelling.*

Molecular models of **1a-d** and **2a-d** were constructed using Chem3D Pro version 11.0 (Cambridgesoft) assuming all-*trans* alkyl chain structures. Structure optimizations were performed using MM2 followed by MOPAC energy minimizations on all models and subsequently the headgroup volumes were recorded and the Connelly excluded volumes calculated and recorded.

**3. Results and Discussion**

*3.1 Syntheses of bolaform amphiphiles.*

Hayman *et al.* have previously described the successful synthesis of amphiphiles **1a**, **2a**, **2b** and **2d** and in this work we report on these and on the additional structures **1b-d** and **2c**.[23] The syntheses of **1a-d** and **2a-d** are given in Scheme 1 and in particular the polar amphiphiles were synthesized by the ring-opening bromination of a naturally-occurring, relatively non–polar, lactone, hexadecanolide **3** *via* nucleophilic attack of the bromide. The product, 15-bromohexadecanoic acid, was either quaternised with a large excess of trialkylamine to form **1a-b** and **1d**, or reduced with borane to form 16-bromohexadecanol, which was then quaternised as before to form **2a-d**. The reactions were conducted either by: method 1, heating the reagents in a sealed tube without solvent at 80°C; or method 2, heating the reagents under reflux conditions in ethanol. Both of these approaches were based on the methods adopted by Hayman *et al.* for the syntheses of **1a**, **2a**, **1b** and **2d**. However neither method resulted in the synthesis of **1c** even when the sealed tube containing the reaction mixture was heated at a higher temperature (100ºC) for method 1 and, butanol was used in place of ethanol (higher bp) for method 2. Results from NMR suggested that in the attempted synthesis of **1c** the step-growth polymerisation of the 16-bromohexanoic acid resulted, giving poly(16-hexanoate) and tripropyl ammonium bromide. To overcome this situation protection of the carboxy group by conversion to a methyl ester prior to quaternization proved successful. 15-bromohexadecanoic acid 4, obtained from hexadecanolide as described previously, was converted with MeOH and H2SO4 into methyl 16-bromohexadecanoate, which was quaternised to form 15-(methoxycarbonyl) pentadecyl tripropyl ammonium bromide. This ester was then converted by heating with KOH and water to **1c** (Scheme 1). The disadvantage to this procedure was that two extra steps (protection and deprotection) were added to the synthesis.

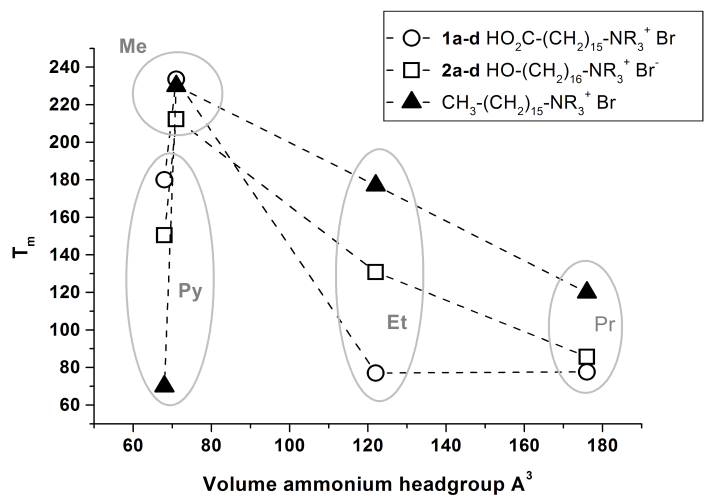


**Scheme 1**

Recrystallization of the crude products gave white crystalline materials which were characterised by 1H NMR spectroscopy, 13C NMR spectroscopy, FT-IR spectroscopy and ESMS.

*3.2 Bolaform Amphiphile Krafft Temperatures (TK).*

The thermal properties of the various bolaform amphiphiles in the solid state were analyzed by differential scanning calorimetry (DSC) between 50 to 250°Cat heating and cooling rates of 10 °C min-1. The DSC thermographs of bolaform amphiphiles **1a-d** and **2a-2d** (supporting information) showed 1, 2 or 3 transitions between 77.0 and 233.6°C upon heating (Table 1) with **2a** and **2d** exhibiting three sharp exothermic peaks and **1a** two sharp exothermic peaks. Observations of these samples under polarized optical microscopy (POM) indicated no mesogenic behavior or textures for any of the crystal phases covering the temperature range in question. The other bolaform amphiphiles showed a single sharp exothermic peak by DSC corresponding to the melting point by POM. The final transition temperatures of all of the compounds corresponded to isotropisation of the compounds (by POM) and for those compounds previously synthesized were comparable to the literature melting points (Table 2).



**Figure 2.** (a) Final melting temperatures of compounds **1a-d** and **2a-d** versus headgroup volume.

Melting points taken from literature show that the trimethyl-, triethyl- and tripropyl-hexadecylammonium bromides display a linear decrease in Tm with head-group size (Figure 2). This is most probably a reflection of the increasing negative effect of the headgroup volume on the ability of the molecules to close pack in the crystal phase. Interestingly the hydroxyl-analogues **2a**-**2c** show a similar trend (though the relationship is not quite linear) whereas the carboxy-derivatives **1a**-**1c** do not. In all cases the melting points of the triethyl- and tripropyl-compounds are lower than the trimethyl as expected when considering packing and headgroup volumes. Despite the similar size in ammonium headgroup volume between the pyridyl- derivatives (68Å3) and the trimethyl- (71Å3) derivatives, the pyridyl compounds do not present any clear trend in melting behaviour when compared to the trialkyl- analogues, or themselves as a series.

TK values were determined for all the bolaform amphiphiles in dilute aqueous solutions (1% w/v) with the TK being recorded when complete dissolution of the sample in a stirred solution was observed. The averages of the TKs obtained from 3 measurements of sample solutions at pH 2.2, 7.0 and 11.5 are given in Figure 3. The TKs for bolaform amphiphiles at pH 7.0 in all cases were 20 to 50°C higher than those for the analogous simple hexadecyl trialkylammonium bromides. This largely correlates with data from Hayman *et al.* with the TKs in general agreement with the previously recorded values (**2a**, **2b**, **2d** and **1a**, Table 3).[22, 30]

Kraft temps combined v3.tif

**Figure 3.** Krafft temperatures for the ω-carboxy bolaform amphiphiles **1a-1d** and ω-hydroxy bolaform amphiphiles **2a-2d**. **1b** was found to have a Krafft temperature above 100°C and consequently could not be accurately measured. Error bars not included (<0.1% standard deviation from 3 measurements).

Of particular note are the low TKs (19.1°C) for **2a** (TMC16OH) and for **1c** (TPrC16CO2H) (21.2°C) which supports observations made of their abilities to form micellar solutions at room temperature. Both compounds have lower TKs than CTAB (TK = 25°C). However the majority of the bolaform amphiphiles tested (**2b-d**, **1a**, **b**,**d**) possessed TKs significantly above those recorded for the analogous hexadecyl trialkyl- and pyridyl- ammonium bromides.[22, 31]The methyl- and pyridyl-carboxy compounds **1a** (TMC16CO2H) and **1d** (PyC16CO2H) show remarkably similar TKs at pH 7.0 (77.4 and 71.8°C) as do the methyl- and pyridyl-hydroxy amphiphiles, **2a** (TMC16OH) and **2d** (PyC16OH) (57.4 and 64.3C°). Differences in TKs of micelle forming compounds usually result from relative differences in the stabilities of their crystal forms and/or differences in their monomer solubilities.[22] The cmcs of the bolaform amphiphiles were measured using 1H NMR according to published procedures where a plot of chemical shift difference (relative to monomer) of the CH, CH2 and CH protons (for pyridyl, ethyl/propyl and methyl respectively) adjacent to the nitrogen in the headgroups versus the inverse of the total surfactant solution concentration yields an intersection of two straight lines and the cmc. A representative plot for **1a** is given in Figure 4 (the other plots are given in Supporting Information) and the results are given in Table 4.

cmc graph Def.tif

**Figure 4.** Chemical shift (relative to monomer) versus 1/C*T* for NCH3 headgroup protons of **2a** in D2O. Cmc taken from the point at which the 2 lines intersect.

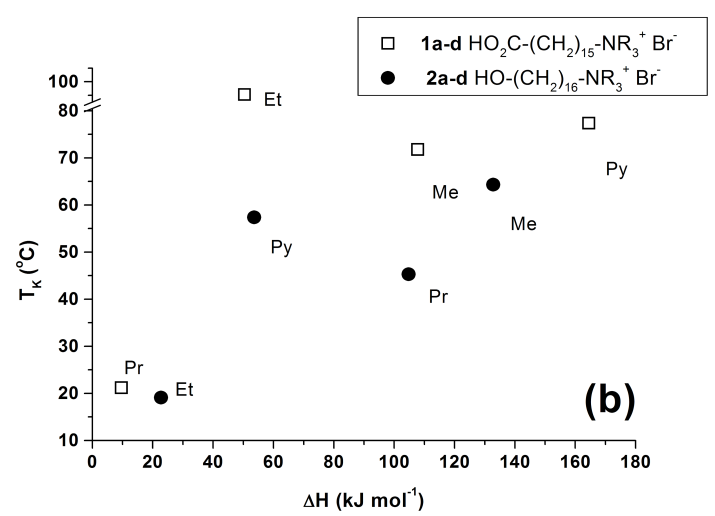
The cmc values for **1a,c, d** and **2a-d** were between 5.4 and 8.6 mmol dm-3, which are approximately 10 times larger than the simple ammonium analogues CTAB, CTEtAB, CTPrAB and CPyAB (Table 3) indicative of significantly higher solubilities in water. Once again our results are in good agreement with previously published results for the existing amphiphiles. The higher solubility of the bolaform amphiphiles is almost certainly a result of their higher overall hydrophilic character and Yasuda *et al.* have observed a decrease in the cmc of eicosane-1,20-bis(trialkylammonium) dibromide following the order from methyl > ethyl > propyl for different alkyl groups (0.82, 0.52 and 0.35 mmolL-1 respectively).[7] This relationship is followed for compounds **2a**-**2c** and between **1a** and **1c** but not for the pyrene compounds **1d** and **2d**. However no clear relationship was observed between TK and cmc for the compounds (Figure 5) and it is possible to conclude that the relative solubility (hydrophobic-lipophilic balance) does not appear to be relevant in predicting TK (in line with the hypothesis of Hayman *et al.*).

Tk vs cmc.tif

**Figure 5.** A plot ofTK versus cmc for the bolaform amphiphiles **1a**,**c**,**d** and **2a-d**.

Therefore it must be assumed that the relative stability of the crystalline state of the bolaform amphiphiles is the principle determinant for the magnitude of their TKs. Hayman *et al*. reported a comparison of the crystal structures of **2a** (TMC16OH) and CTAB which both possessed head to tail interdigitated structures with the alkyl chains aligning parallel to one another.[22] In addition to the quaternary ammonium bromide ion-ion interaction seen for CTAB, **2a** was also suggested to display hydrogen bonding between the hydroxyl and the bromide counter-ion and an ion-dipole interaction between the hydroxyl and the quaternary ammonium ion. These additional stabilizing interactions for the crystal structure of **2a** were postulated to be responsible for its increased TK (66°C) when compared to CTAB (25°C). Furthermore the additional CH2 units on the triethyl- derivatives **2b** (TEtC16OH) and CTEtAB were postulated to disrupt the ion-ion interaction for both compounds and in addition reduce the strengths of the hydrogen bond and ion-dipole interactions in the crystal state for **2b** resulting in decreased TK values(<0°C for CTEtAB and 18°C for **2b**). Crystalline stability is directly related to the melting point and enthalpies of the phase transitions of compounds and it has previously been postulated that within a series of amphiphilic compounds that melting points may be correlated with Krafft temperatures.[22] A plot of Tm taken from the thermal analyses of the bolaform amphiphiles (Table 2) versus TK for these amphiphiles is given in Figure 6a and the plot of TK versus of the total enthalpy for all transitions between 50°C and Tm is given in Figure 6b.

Tk vs Tm.tif



DHxTMvsTK.tif

**Figure 6.** Variation in Krafft temperatures with (a) melting points, (b) enthalpies and (c) the product of TM and H for compounds **1a-d** and **2a-2d**.

As can be seen there is some correlation between Tm and TK for all compounds with the exception of **1b** (TEtC16CO2H) and a rougher correlation between TK and H for all compounds again with the exception of **1b**. Generally the lower the Tm and/or H the lower the TK. To attempt to take both H and Tm into account in predicting TK a plot of the product of these two properties is given in Figure 6c. A considerable reduction in scatter and a clear trend is observed with the exception of **1**; a 1st order exponential decay curve fit gives TK ∝ exp(H\*TM). These observations support the hypothesis of Hayman *et al.* that the stability of the crystal state of an amphiphile is the principle factor in determining it’s TK and the relationship between TK and H\* Tm is worthy of consideration in the future prediction of Krafft temperatures. However the clearly anomalous behaviour of compound **1b** remains unexplained.

One application of ,-hydroxyhexadecyl trialkylammonium bromides is to act as the template in super-microporous silicate syntheses. This occurs via condensation of silicate anions or tetralkoxysilane under acidic or basic conditions and consequently it was felt necessary to determine if any significant changes in TK of our bolaform amphiphiles occurred under these conditions. Surprisingly only a single study has previously reported on the effect of pH on the TKs of long chain alkyl ammonium salts.[32] In that case it was reported that an increase in pH led to a decrease in the TK of dodecyl ammonium chloride. The TKs were measured for all of our compounds at pH 2.2 and 10.5 where the results were given in Figure 3. The differences in TK in these pHs and those recorded at at pH 7.0 are given in Figure 7. It can be observed that for almost all of the compounds the differences in pH resulted in an increase in TK. Given the ionisable nature of carboxylic acid function it was surprising that pH had greater overall effect on the TKs of the hydroxyl- (**2a-d**) compared to the carboxy-compounds (**1a-d**). The fact that it was observed that the greater differences occurred for those amphiphiles with different ammonium head-groups suggests that the structure of these moieties plays a greater role in defining the Krafft temperature than the hydroxyl or carboxy groups. However it has been reported that the nature of the counter-anion and concentration of salts in the aqueous solvent strongly influences Krafft temperatures for ammonium amphiphiles and such ionic effects may have greater effect than the pH.[33-35] Generally it has been observed that increased salt concentrations in the aqueous solvent leads to higher TKs for ammonium amphiphiles and this is observed fro all but one of the bolaform amphihiles (**2d**).

DeltaTK vs pH.tif

**Figure 7.** Effect of pH on the Krafft temperatures of compounds **1a-d** and **2a-d** with respect to pH 7.0.

*3.3 The Nature of the Bolaform Amphiphile Aggregates*

The aggregation numbers (Nagg) ofcompounds **1a,c,d** and **2b-d** in D2O weredetermined using an NMR technique to measure the chemical shifts of the CH3, CH2 or CH protons adjacent to the ammonium ion of the headgroups, through a series of dilutions. Nagg values were determined using the single-step equilibrium model where a plot of ln(*C*Tδobs) against ln[*C*T(δmic – δobs)] gives a straight line with a slope equal to the aggregation number *Nagg*.[21], [36-38] An example of a plot resulting from the measurements is shown in Figure 8 for the amphiphile **2c** (further plots are given in Supporting Information). Nagg for **1b** could not be determined because of its high TK but the aggregation numbers of **1a,c,d** and **2a-d** are given in Table 5. Our values for **2a**, **2b**, **2d** and **1a** are in good agreement with those previously obtained by Haymann *et al.* (Table 5) and all of the amphiphiles clearly showed substantially smaller aggregation numbers (Nagg = 2.9 to 6.7) than their analogous hexadecyl ammonium bromides (Nagg = 43 to 104) (Table 5).

Dynamic light scattering was used to measure the apparent hydrodynamic diameters (DH) of compounds **1a, 1c, 1d** and **2a-d** as 1wt% (> cmc) aqueous solutions and representative overlays of frequency counts are given in Figure 9 and the average results are given in Table 5. It can be observed that the carboxylic acid amphiphiles (**1a, c, d**) have apparent hydrodynamic diameters approximately *twice* those of the hydroxy-bolaform amphiphiles (**2a-d)**. To determine Nagg from the DH values required an estimation of the molecular volumes of the bolaform amphphiles and whilst a number of values exist in the literature

TPC16OH Agg number.tif

**Figure 8**. Representative plot of ln(*C*Tδobs) against ln[*C*T(δmic – δobs)] for **1c** (TPC16OH); the aggregation number was determined from the slope of the linear regression.

for volume group contributions to molecular volumes of surfactants, [39], [40-48] the consistent data reported by Lepori and Gianni in their experiments were used in the calculation of V1calc andN1agg;[49] for comparison the Connelly excluded volumes (calculated using Chem3D from Cambridgesoft) were used in the calculation of V2calc and N2agg (Table 5). The volumes of the aggregates were calculated from the DH values (4/3(DH/2)3) and the are therefore the theoretical maximum values from the DLS measurements. The N1agg and N2agg values for **2a-d** are of the same order of magnitude as those determined by NMR whilst those for **1a-d** are significantly larger than those determined by NMR.

DLS overlays.tif

**Figure 7.** Typical aggregate size (volume) distributions measured using DLS.

The chain length (l) for the hydrocarbon chains of **1a-d** and **2a-d** can be calculated from l = 0.2765 + 0.1265\*nCH2 [47, 50] which gives l = 2.3 nm (ignoring headgroup contributions). Previous studies on chains in simple single alkyl chain bolaform amphiphilic micelles and at the air-water interface have given contradictory results. Zana *et al.* gave evidence for the adoption of a ‘hair-pin’ conformation of the alkyl chain where the chain adopts gauche turns in the alkyl chain region leading to a U-shape allowing both polar groups to orientate towards the water interface (see Figure 8).[10, 12] In contrast Yasuda *et al.* and other groups have presented evidence for extended (or stretched) chain conformations.[5-8] Irrespective of whether folded or extended conformations are adopted, this diameter (2.3 nm) is close to the maximum for a micelle formed from these amphiphiles and is approximately half the diameter of a typical CTAB micelle (Figure 1). This maximum micellar diameter corresponds to approximate aggregation numbers of between 20 to 30. It is noticeable that the carboxy- amphiphiles appear to form micelles with diameters close to this maximum whilst those of the hydroxyl- amphiphiles are significantly smaller. Since Nagg values measured from NMR by us and Hayman *et al.[21]* are similarly low, these results suggest that the aggregates formed from hydroxy amphiphiles **2a-d** have close packed chains whereas the acid amphiphiles, **1a**,**c** and **d** possess significantly less densely packed chains. This picture is summarized schematically in Figure 9. We can think of no obvious explanation for these differences in the aggregate sizes and packing between the hydroxy- and carboxy- amphiphiles. One possibility for the origin of the larger aggregates of **1a**,**b** and **d** would be steric crowding at the aggregate-water interface for the ammonium and acid groups forcing an expanded interface relative to volume. However the calculated aggregation numbers (N3agg in Table 3) based on the calculated surface area (A) calculated from the DH values and on headgroup molecular areas taken from surface tension measurements in the literature,[51], [52-54] suggest that this is not an issue since the N3agg values are close to those predicted by volume calculations (i.e. N3agg ≈ N2agg).

pKa can be used to gauge the extent of ionisation of acid groups and also provide insight into the relative proximity of the carboxylate or acid groups at the micelle-water interface but **1b** and **1c** were not soluble in the MeOH/water solvent used and their pKas could not be determined. The pKas of the -hydroxy bolaform amphiphiles **2a-d** could also not be determined as primary aliphatic hydroxyl groups have pKas of around 15 to 17,[55-57] beyond the range that could be determined by the potentiometric technique employed. The pKa values of **1a** (TMC16CO2H) and **1d** (PyC16CO2H) were however determined by potentiometric methods and were found to be 4.34 and 4.41 respectively. The pKa values for hexadecanoic acid and octanoic acid are ~8.7 and 4.9 respectively.[58] As chain lengths increase in a series of carboxylic acids the increased van der Waals interactions between the chains of adjacent molecules lead to closer packing of the chains and the acid groups within any micellar aggregates;[58] the cumulative effect is increased shielding of the hydrogen atom between the two oxygen atoms of adjacent acid groups and higher pKa values. Conversely the greater the distance between carboxylate/carboxylic acid groups, the lower the p*Ka* value of the acid. In the case of the bolaform amphiphiles **1a** and **1d** the presence of the polar ammonium groups may have the effect of decreasing shielding of the hydrogen atom between acid groups which might account for their lower pKa results when compared to their non head-group derivatised analogues. It has also been reported that the incorporation of very hydrophobic alkanoic acids (e.g. hexanoic and octanoic acids) into micelles of CTAB leads to the presence of the carboxylic acid and the ammonium groups at the surface.[59] The presence of both acid and ammonium groups at the micelle surface has the effect of stabilizing the whole micelle by acid ionization and furthermore increasing the acidity of the solutions (compared to pure solutions of the acids) by charge neutralization of the carboxylate.

It has been previously observed for micellar solutions of hexadecane-1,16-bis(trimethylammonium bromide) that considerable water penetration occurs into the ‘hydrophobic’ core – so much so that it was questioned whether a hydrophobic core truly existed in these systems.[10] The presence of carboxylate and ammonium charged groups at the micelle surface for the carboxy- bolaform amphiphiles may lead to a similarly high degree of water complexation about the headgroups in the interfacial region. In contrast it has been observed for mixed systems of ammonium surfactants and various aliphatic alcohols that interactions between the OH group and the headgroup of ammonium surfactants reduced the electrostatic repulsion between neighbouring headgroups and lead to a greater exclusion of water from this interfacial region (as demonstrated by micropolarity measurements).[60] Thus the difference in apparent diameters of the hydroxyl- and carboxy- amphiphiles aggregates might be a consequence of an expanded interfacial surface for the ammonium-acid compounds and a reduced interfacial surface for the ammonium-hydroxy compounds, determined by the relative degree of water molecule association in the Stern and possibly palisade layers. This model is illustrated schematically in Figure 9.

A further important feature in all of DLS measurements was the monomodal nature of the aggregates, whilst larger peaks were observed (~100nm and ~1000nm) through intensity measurements these became insignificant after number and volume calculations were performed. No aggregates were conclusively observed by cryo-TEM (micrographs of **2a**, **2b** and **2d** can be found in Supporting Information) though objects circa 1 nm in diameter were possibly present. Thus for all cases a single sized aggregate species is present (>99% in

acid vs alcohol micelles.tif

**Figure 9.** Tentative models for the micellar aggregates formed by **1a** and **2a**.

number) with diameters of less than 3nm (by DLS and TEM) and Nagg < 10. This in contrast to the results of Jaeger *et al.* who reported the formation of fibres from **1a**, however these observations were made in buffered solutions.[29] The IUPAC definition of a micelle is “an aggregate with colloidal dimensions (at least one dimension in the range 1nm to 1m) formed from a surfactant in solution which exists in equilibrium with the molecules or ions from which it is formed”. Under this definition the aggregates formed from the bolaform amphiphiles **1a**,**1b**, **1d** and **2a-d** can be described as micelles albeit with very low aggregation numbers (Nagg<10).

**4. Conclusions**

It has been possible to synthesise 8 bolaform compounds and undertake their systematic characterization. Overall the TKs of the eight amphiphiles were high with 6 of the 8 possessing TKs greater than 45ºC. Thus most of the amphiphiles could only expect to find application at raised temperatures limiting their potential utility. However in addition to ,-hydroxy-hexadecyl triethylammonium bromide (**2b**) with a TK of 19.1°C, another amphiphile, ,-carboxy-hexadecyl tripropylammonium bromide (**2c**) has been identified with a TK near ambient temperatures, TK of 22.1°C. This provides an acid functional ammonium bolaform amphiphile that micellises at ambient tempratures to complement the hydroxyl. No definitive relationship was observed between the TKs of the 8 bolaform amphiphiles and the structure of their headgroups and no correlation between the amphiphile cmcs and TKs was observed. A good correlation between TK and the product of the enthalpies and melting temperatures of the compounds was observed for 7 of the 8 compounds, but further and more extensive experiments are needed to determine the general validity of this observation. These observations support previous observations that TKs are determined by the crystal stability of the bolaform amphiphiles rather than their relative solubilities. Considerable change of the amphiphiles TKs for different pHs (pH = 2.2 and pH = 11.5) was observed. For 7 of the compounds pH either had no effect or increased TK by up to 20ºC; the remaining compound showed a decrease in TK. Thus considerable care needs to be taken in applying these compounds under basic or acidic conditions. No clear trends were observed for the compounds despite the obvious differences in ionisability of the carboxylic acid and hydroxyl functions.

The cmcs recorded for the amphiphiles were observed to be an order of magnitude larger than those for analogous mono-ammonium amphiphiles with little difference in cmcs between the hydroxyl- and carboxy-containing compounds. Generally with the exception of the pyridyl compounds the larger the ammonium headgroup the lower the cmc and the aggregation numbers of all compounds (excepting **1b**) were very low (Nagg<10). The apparent micellar diameters for the hydroxyl-bolaforms (**2a-d**) were in the range 1.0-1.4 nm whereas those for the carboxy-compounds (**1a**, **1c**, **1d**) were in the range 2.1-2.4 nm. Given the low Nagg values and the significant differences in micellar volumes, this suggests a considerable difference in the packing of the two sets of amphiphiles with loose low density aggregates or ‘molecular clusters’ for the carboxy compounds and more dense micellar type aggregates for the hydroxyl-compounds. We postulate that his most likely results from different degrees of water penetration of the micelles. In both cases however the sizes and the low aggregation numbers point suggest that these aggregates are more characteristic of the pre-micellar aggregates observed for many amphiphiles but in particular gemini surfactants which often appear to exist with low aggregation numbers (dimers, trimers etc).[58, 61-67]

**Acknowledgment**

The authors thank the European Commission for financial support under FP6 (NACBO 500804).

**Supporting Information Available**. Supporting information includes representative DSC chromatograms, thermal data from DSC cooling runs and all plots used to obtain cmc values and Nagg values form NMR measurements.

**References**

**Table 1.**

Reaction conditions and yields of **1b** and **1d**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| ***Product*** | ***Alkyl bromide*** | ***Amine*** | ***Reflux time*** | ***Recrystallisation solvent(s)*** | ***Yield*** |
| 1b | 4.96 g (1.9 mmol) | Triethylamine | 4 days | 1. Ethanol, diethyl ether  2. Ethanol, diisopropyl ether | 2.2 g (42%) |
| 1d | 5.88 g (0. 3 mmol) | Pyridine | 13 hours | Methanol, water | 1.8 g (31%) |

**Table 2.** Transition temperatures (°C) and enthalpies (J g-1) of compounds **1a**-**1d** and **2a**-**2d** by DSC.

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Cmpd.** | **Tm(1)** | **ΔH(1)** | **Tm(2)** | **ΔH(2)** | **Tm(3)** | **ΔH(3)** | **Lit. Mpa** | **Mpb** |
| **1a TMC16CO2H** | 196.9 | 41.5 | 233.6 | 66.3 | - | - | 218c | 230c (CTAB) |
| **1b TEtC16CO2H** | 77.0 | 50.4 | - | - | - | - | na | 177c (CTEAB) |
| **1c TPrC16CO2H** | 77.7 | 9.6 | - | - | - | - | na | 120d (CTPrAB) |
| **1d PyC16CO2H** | 180.0 | 164.5 | - | - | - | - | na | 70c (CPyAB) |
| **2a TMC16OH** | 113.2 | 20.8 | 150.2 | 46.8 | 212.3 | 65.2 | 217c | 230c |
| **2b TEtC16OH** | 130.9 | 22.8 | - | - | - | - | 159c | 177c |
| **2c TPrC16OH** | 85.7 | 104.8 | - | - | - | - | na | 120d |
| **2d PyC16OH** | 92.6 | 38.6 | 132.0 | 13.8 | 150.5 | 1.22 | 155c | 70c |

a. Literature melting points of ω-hydroxy and ω-carboxy hexadecyl trialkyl (or pyridyl) ammonium bromides. b. Melting points of hexadecyl trialkyl (or pyridyl) ammonium bromides. c. Taken from reference  [22]. d. Taken from reference [39].

**Table 3.** Krafft temperatures for compounds **2a**, **2b**, **2c** and **1a** compared with those in literature.

|  |  |  |
| --- | --- | --- |
| **Compound** | **TK (°C) (this work)** | **TK (°C)a (literature)** |
| **2a** TMC16OH | 64.3 | 66 |
| **2b** TEC16OH | 19.1 | 18 |
| **2d** PyC16OH | 57.4 | 55 |
| **1a** TMC16CO2H | 71.8 | 65 |

a. Taken from reference 22 [22].

**Table 4.** Critical micelle concentrations **1a**,**c**,**d** and **2a-2d.**

|  |  |  |
| --- | --- | --- |
| **Compound** | **Cmc/mmol dm-3** | |
| This study | Lit. |
| **CTAB** | - | 0.86 - 1.55a |
| **CTEAB** | - | 0.73b |
| **CTPAB** | - | 0.14-0.58c |
| **PyC16Cl** | - | 0.67-1.38d |
| **1a TMC16CO2H** | 7.4 | 9.7e |
| **1b TEtC16CO2H** | - | - |
| **1c TPrC16CO2H** | 5.4 | - |
| **1d PyC16CO2H** | 6.0 | - |
| **2a TMC16OH** | 8.6 | 9.4e |
| **2b TEtC16OH** | 6.2 | 6.2e |
| **2c TPrC16OH** | 5.4 | - |
| **2d PyC16OH** | 6.0 | 5.9e |

a. Taken from references[21], [30], [68]. b. Taken from references [51, 63]. c. Taken from references [51, 69, 70]. d. Taken from references [21],[68]. e. Taken from reference [21].

**Table 5.** Aggregation numbers measured by NMR and taken from literature sources, apparent aggregate diameters (DH) determined from DLS for compounds, calculated volumes and theoretical aggregation numbers.

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Compound** | **Nagg *(NMR)*** | | **DH/Å *c*** | **V1calc**  **/nm3 d** | **Theor. N1agg e** | **V2calc /nm3 *f*** | **Theor. N2agg g** | **Aagg/nm2 h** | **Theor. N3agg i** |
| This studya | Lit.*b* |
| **CTAB** | - | 88-104, 61, 69 | - | - | - | - | - |  |  |
| **CTEtAB** | - | 43, 60 | - | - | - | - | - |  |  |
| **CTPrAB** | - | 40-70, 53 | - | - | - | - | - |  |  |
| **CPyAB** | - | 95 | - | - | - | - | - |  |  |
| **1a TMC16CO2H** | 3.9 (0.1) | 6±4 | 2.33 (0.58) | 0.356 | 18.7 | 0.228 | 28.3 | 17.1 | 28.0 |
| **1b TEtC16CO2H** | - | - | - | - | - | - | - | - | - |
| **1c TPrC16CO2H** | 3.5 (0.8) | - | 2.10 (0.16) | 0.456 | 10.6 | 0.257 | 18.1 | 13.8 | 13.8 |
| **1d PyC16CO2H** | 2.9 (0.1) | - | 2.36 (0.03) | 0.358 | 19.3 | 0.288 | 23.0 | 17.6 | 27.4 |
| **2a TMC16OH** | 5.9 (1.4) | 5±2 | 1.21 (0.36) | 0.354 | 2.6 | 0.234 | 4.0 | 4.60 | 7.7 |
| **2b TEtC16OH** | 6.7 (1.7) | 11±2 | 1.44 (0.36) | 0.404 | 3.9 | 0.229 | 6.8 | 6.51 | 7.8 |
| **2c TPrC16OH** | 2.9 (0.1) | - | 1.07 (0.12) | 0.454 | 1.4 | 0.267 | 2.4 | 3.59 | 3.6 |
| **2d PyC16OH** | 4.7 (0.3) | 9±2 | 1.00 (0.02) | 0.356 | 1.5 | 0.300 | 1.8 | 3.16 | 5.0 |

*a.* Standard deviation given in brackets. *b.* Values taken from references[30, 31],[71, 72] *c.* Hydrodynamic diameter (volume) measured by DLS (average 3+ measurements) at >5°C above TK; standard deviation given in brackets. *d.* Molecular volumes of bolaform amphphiles calculated from partial molar volumes in ref [49].*e*. N1agg =( 4/3(DH/2)3)/V1calc. *f*. Connelly excluded volumes of bolaform amphphiles calculated using Chem3D (Cambridgesoft). *g*. N2agg = (4/3(DH/2)3)/V2calc *h*. Aagg = 4(DH/2)2 *i*. N3agg=(Aagg/Aheadgroups) where Aheadgroup = head group limiting areas taken from [60], [52-54]

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