

Headgroup effects on the krafft 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 synthesised and characterised; 4 α,ω -hydroxy-alkane trialkyl (and pyridyl) ammonium bromides and 4 α,ω -carboxy-alkane trialkyl (and pyridyl) ammonium bromides where the alkyl groups were methyl, ethyl and propyl. Four of these represented new compounds. Overall the Krafft temperatures (T_K) of the eight amphiphiles were high, with 6 of the eight possessing T_K s greater than 45 °C. 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 α,ω -hydroxy-hexadecyl triethylammonium bromide (**2b**) with a T_K of 19.1 °C, another amphiphile, α,ω -carboxy-hexadecyl tripropylammonium bromide (**2c**) has been identified with a T_K near ambient temperatures (T_K of 22.1 °C). This provides an acid functional ammonium bolaform amphiphile that micellises at ambient temperatures to complement the hydroxyl derivative. A correlation between T_K and the product of the enthalpies and T_m s of the compounds was observed for 7 of the eight compounds. No correlation between the amphiphile critical micelle concentrations (cmc) and T_K s was observed confirming previous reports that T_K values are predominantly determined by crystalline stability rather than solubility. Considerable differences were observed between the various amphiphile T_K s 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 ionised). 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 (N_{agg}) obtained for all compounds were very low ($N_{agg} < 7$) and the apparent micellar diameters for the hydroxyl-bolaforms were in the range 1.0–1.4 nm whereas those for the carboxy-compounds were in the range 2.1–2.4 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 denser 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.

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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 and Edelson [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

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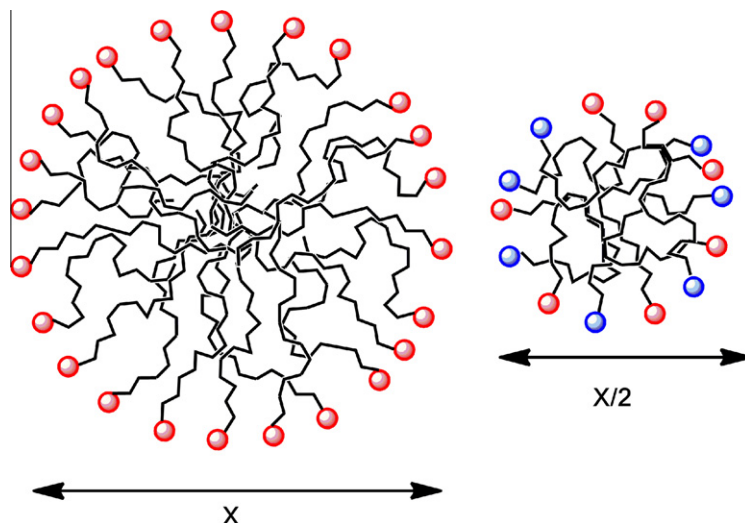


Fig. 1. Idealised schematic illustration of difference in size between standard micelle from mono-functional alkyl compound and a bolaform amphiphile.

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 (Fig. 1).

Increasing interest has been paid to non-symmetrical α,ω -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 α,ω -hydroxy-alkane trialkylammonium bromides and a single α,ω -carboxy-alkane trialkylammonium bromide and further reported on the Krafft temperatures (T_K) 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 and 2.0 nm (termed supermicroporous 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.); four new and four previously synthesised ω -hydroxy and ω -carboxy hexadecyl quaternary ammonium 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 bolaform ammonium surfactant solutions needed to be determined: (i) T_K 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 T_K 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 sulphide complex, hydrobromic acid (48%), ammonium hydroxide (28–30%) and ethyl acetate (99.8%) were purchased from Aldrich. Sulphuric acid (H_2SO_4) (98%), dichloromethane (DCM) (99.99%, analytical grade), sodium chloride, water (analytical grade), magnesium sulphate (MgSO_4) (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 and tetramethyl ammonium hydroxide 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 purchased from GOSS Scientific Instruments Ltd. Tetrahydrofuran (THF) (99.5%, analytical grade, Fisher) was pre-dried over magnesium sulphate and sodium wire, then distilled over sodium wire and benzophenone immediately prior to use. Potassium chloride was purchased from Carlo Erba Reagents.

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 ^{13}C NMR spectra were recorded in 5 mm NMR tubes using a

JEOL GX-270FT at 270 MHz at 30 °C 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. Infrared 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 5–10 min at room temperature. The solution was then diluted 1:10 ratio 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 (1.2–1.4 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 μ l aluminium crimped pans were used. The baseline was corrected by using two empty aluminium crimped pans and the sample was prepared by crimping 10–20 mg of the sample.

2.3. Syntheses

2.3.1. 16-bromohexadecanoic acid

16-Bromohexadecanoic acid was synthesised using the method published by Chuit and Hauser for the synthesis of 15-bromopentadecanoic acid [27]. Hexadecan-16-olide (24 g, 50 mmol) was added to concentrated HBr (56 ml) and sulphuric acid (15 ml) in a 100 ml round-bottomed flask and heated under reflux for 3½ 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, BrCH₂), 2.35 ppm (t, 3H, HO₂CCH₂), 1.85 ppm (m, 5H, BrCH₂CH₂), 1.63 ppm (m, 5H, HO₂CCH₂CH₂), 1.13–1.49 ppm (m + s at 1.26 ppm, 22 H, BrCH₂CH₂(CH₂)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).

2.3.2. 16-bromohexadecan-1-ol

16-Bromohexadecan-1-ol was prepared by borane reduction of the corresponding bromo-acid according to the method published by DeVries 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 h at ambient temperature after which the 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, BrCH₂), 3.41 ppm (t, 3H, BrCH₂), 1.86 ppm (m, 5H, BrCH₂CH₂), 1.57 ppm (m, 5H, HOCH₂CH₂), 1.11–1.47 ppm (m + s at 1.26 ppm, 22H, BrCH₂CH₂(CH₂)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).

2.3.3. 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 Davey and Hayman [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 M equivalents of trimethylamine and heated at 80 °C 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⁺CH₂), 3.19 ppm (s, 9H, (CH₃)₃N⁺CH₂), 2.29 ppm (t, 2H, HO₂CCH₂), 1.76 ppm (m, 2H, (CH₃)₃N⁺CH₂CH₂), 1.61 ppm (m, 2H, HO₂CCH₂CH₂), 1.12–1.45 ppm (m + s at 1.27 ppm, 22H, HO₂CCH₂CH₂(CH₂)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, (CH₃CH₂)₃N⁺CH₂), 3.64 ppm (m, 6H, (CH₃CH₂)₃N⁺CH₂), 2.32 ppm (t, 2H, HO₂CCH₂), 1.63 ppm (m, 4H, (N⁺CH₂CH₂(CH₂)₁₁CH₂), 1.12–1.45 ppm (m + t at 1.21 ppm, 31H, (CH₂)₁₁CH₂N⁺(CH₂CH₃)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⁺CH₂CH₂), 2.29 ppm (t, 2H, HO₂CCH₂), 2.04 ppm (m, 2H, N⁺CH₂CH₂), 1.61 ppm (m, 2H, HO₂CCH₂CH₂), 1.12–1.45 ppm (m + s at 1.27 ppm, 22H, HO₂CCH₂CH₂(CH₂)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.

2.3.4. 15-carboxy-N,N,N-tripropylpentadecan-1-ammonium bromide (**1c**)

Difficulties were encountered following the procedure published by Davey and Hayman [23]. However, **1c** was successfully synthesised using a 3-step synthesis (protection, quaternisation and deprotection) following published procedures (see Section 3) as follows [29].

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, di-iso-propyl ether	2.2 g (42%)
1d	5.88 g (0.3 mmol)	Pyridine	13 h	Methanol, water	1.8 g (31%)

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 h 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 purified by column chromatography on a 20 cm × 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, $\text{CH}_3\text{O}_2\text{C}$), 3.38 ppm (t, 2H, BrCH_2), 2.28 ppm (t, 2H, $\text{CH}_3\text{O}_2\text{CCH}_2$), 1.83 ppm (m, 2H, BrCH_2CH_2), 1.59 ppm (m, 2H, $\text{O}_2\text{CCH}_2\text{CH}_2$), 1.08–1.46 ppm (m + s at 1.23 ppm 22H, $\text{O}_2\text{CCH}_2\text{CH}_2(\text{CH}_2)_{11}$).
2. **(15-(methoxycarbonyl)pentadecyl)trimethyl ammonium bromide.** A mixture of 16-bromohexadecanoate 1.23 g, 35.1 mmol and tripropylamine (6.6 ml) were heated in a sealed tube at 80 °C 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, $(\text{CH}_3\text{CH}_2\text{CH}_2)_3\text{N}^+\text{CH}_2$), 2.30 ppm (t, 2H, $\text{CH}_2\text{COOCH}_3$), 1.53–1.90 ppm (m, 10H, $(\text{CH}_3\text{CH}_2\text{CH}_2)_3\text{N}^+\text{CH}_2\text{CH}_2(\text{CH}_2)_{11}\text{CH}_2$), 1.15–1.46 ppm (m + s at 1.25 ppm, 22H, $\text{CH}_3\text{O}_2\text{CCH}_2\text{CH}_2(\text{CH}_2)_{11}$), 1.07 ppm (t, 9H, $(\text{CH}_3\text{CH}_2\text{CH}_2)_3\text{N}^+$).
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, CH_2COOH), 3.33 ppm (m, 8H, $(\text{CH}_3\text{CH}_2\text{CH}_2)_3\text{N}^+\text{CH}_2$), 1.46–1.92 ppm (m, 8H, $(\text{CH}_3\text{CH}_2\text{CH}_2)_3\text{N}^+\text{CH}_2\text{CH}_2$), 1.14–1.43 ppm (m + s at 1.22 ppm, 24H, $(\text{CH}_2)_{11}\text{CH}_2\text{CH}_2\text{COOH}$), 1.04 ppm (t, 9H, $(\text{CH}_3\text{CH}_2\text{CH}_2)_3\text{N}^+$). ^{13}C 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 (CH_2). Anal. Calcd. for $\text{C}_{25}\text{H}_{52}\text{BrNO}_2$: 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).

2.3.5. 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 Davey and Hayman [23]. **2a** was synthesised whereby a mixture of 8.0 g (0.62 mmol) of 16-bromohexadecanol was combined with 10 M equivalents of trimethylamine and heated at 80 °C 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, CH_2OH), 3.20 ppm (s, 9H, $(\text{CH}_3)_3\text{N}^+\text{CH}_2$), 1.76 ppm (m, 2H, N^+CH_2), 1.55 ppm (m, 2H, $(\text{CH}_3)_3\text{N}^+\text{CH}_2\text{CH}_2$), 1.15–1.45 ppm (m + s at 1.27 ppm 22H, $\text{HOCH}_2\text{CH}_2(\text{CH}_2)_{11}$). ^{13}C 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 (CH_2). IR 3345.7 cm^{-1} (O–H), 2915.7 cm^{-1} and 2847.9 cm^{-1} (C–H). Anal. Calcd. for $\text{C}_{19}\text{H}_{42}\text{BrNO}$: 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 M equivalents of pyridine and heated at 80 °C in a sealed tube for 13 h. 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, ($\text{N}^+\text{CH}_2\text{CH}_2$), 3.57 ppm (t, 2H, HOCH_2),

2.04 ppm (m, 2H, $\text{N}^+\text{CH}_2\text{CH}_2$), 1.00–1.68 ppm (m + s at 1.26 ppm, 26H, $\text{HOCH}_2\text{CH}_2(\text{CH}_2)_{12}$). ^{13}C 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 (CH_2). IR 3381.2 cm^{-1} (O–H), 2912.4 cm^{-1} and 2846.8 cm^{-1} (C–H). Anal. Calcd. for $\text{C}_{19}\text{H}_{38}\text{BrNO}$: C, 62.98; H, 9.57. Found: C, 58.56; H, 9.53.

2.3.6. 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 Davey and Hayman [23]. **2b** was synthesised whereby a mixture of 3.5 g (10.9 mmol) of 16-bromohexadecanol was combined with 10 M 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 mixture of ethanol/diethyl ether and then ethanol/di-iso-propyl ether to yield 1.9 g (42%) of **2b**: mp (DSC) 130.9 °C. ^1H NMR δ 3.64 ppm (m, 2H, CH_2OH), 3.53 ppm (m, 6H, $(\text{CH}_3\text{CH}_2)_3\text{N}^+$), 3.27 ppm (m, 2H, $(\text{CH}_3\text{CH}_2)_3\text{N}^+\text{CH}_2$), 1.50–1.77 ppm (m, 4H, $\text{CH}_2(\text{CH}_2)_{12}\text{CH}_2$), 1.15–1.45 ppm (m, 33H, $(\text{CH}_2)_{12}\text{CH}_2\text{CH}_2\text{N}^+(\text{CH}_2\text{CH}_3)_3$); IR 3268.1 cm^{-1} (O–H), 2914.9 cm^{-1} and 2848.2 cm^{-1} (C–H). Anal. Calcd. for $\text{C}_{22}\text{H}_{48}\text{BrNO}$: C, 62.53; H, 11.45. Found: C, 61.89; H, 11.94. ^{13}C 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 (CH_2).

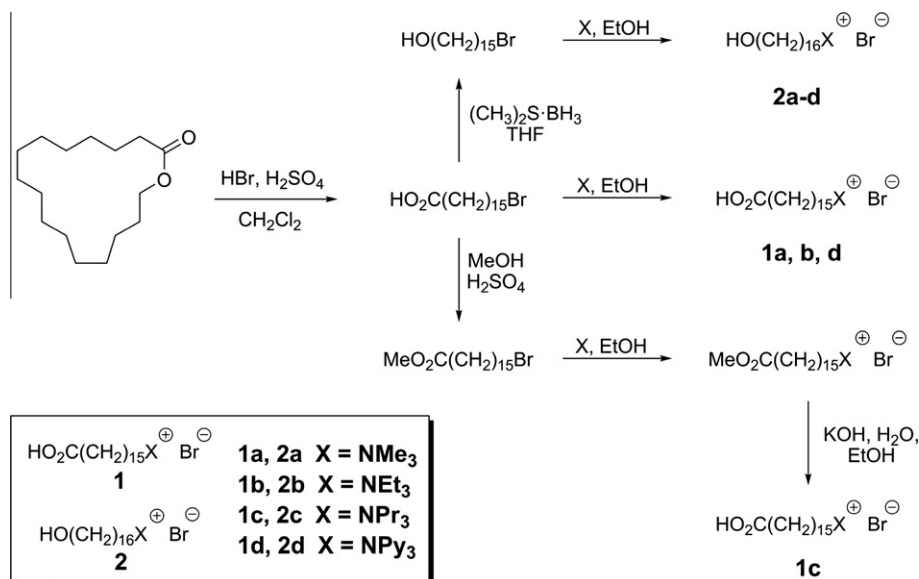
2c was synthesised whereby a mixture of 1.5 g (5.9 mmol) of 16-bromohexadecanol was combined with 10 M equivalents of tripropylamine and heated under reflux in ethanol for 5 days. The reaction mixture was then filtered and the solid obtained was recrystallised from a mixture of ethanol/diethyl ether 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, CH_2OH), 3.37 ppm (m, 9H, $(\text{CH}_3\text{CH}_2\text{CH}_2)_3\text{N}^+\text{CH}_2$), 1.50–1.88 ppm (m, 8H, $(\text{CH}_3\text{CH}_2\text{CH}_2)_3\text{N}^+\text{CH}_2\text{CH}_2$), 1.14–1.45 ppm (m + s at 1.26 ppm, 26H, $(\text{CH}_2)_{12}\text{CH}_2\text{CH}_2\text{OH}$), 1.07 ppm (t, 9H, $(\text{CH}_3\text{CH}_2\text{CH}_2)_3\text{N}^+$). ^{13}C 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 (CH_2). IR 3271.0 cm^{-1} (O–H), 2915.0 cm^{-1} and 2848.0 cm^{-1} (C–H). Anal. Calcd. for $\text{C}_{25}\text{H}_{54}\text{BrNO}$: C, 64.62; H, 11.72. Found: C, 64.20; H, 11.98.

2.4. Krafft temperature determination (T_K)

The Krafft temperatures of the bolaform amphiphiles were determined at pH 2.2, 7.0 and 11.5. Samples were prepared for T_K 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 KHCO_3 , 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 (0.5–5.0 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 270 MHz in D_2O 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



Scheme 1.

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 microscope. 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 optimisations were performed using MM2 followed by MOPAC energy minimisations on all models and subsequently the headgroup volumes were recorded and the Connolly excluded volumes calculated and recorded.

3. Results and discussion

3.1. Syntheses of bolaform amphiphiles

Davey and Hayman 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 synthesised 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 (100 °C) for method 1 and, butanol was used in place of ethanol (higher bpt) 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 quaternisation 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.

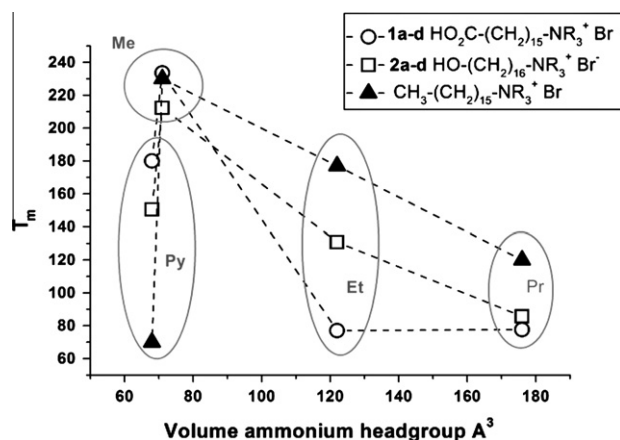
Recrystallisation of the crude products gave white crystalline materials which were characterised by ¹H NMR spectroscopy, ¹³C NMR spectroscopy, FT-IR spectroscopy and ESMS.

3.2. Bolaform amphiphile krafft temperatures (*T_K*) and critical micelle concentrations *cmc*s)

The thermal properties of the various bolaform amphiphiles in the solid state were analysed by differential scanning calorimetry (DSC) between 50 and 250 °C at 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 polarised optical microscopy (POM) indicated no mesogenic behaviour or

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

Cmpd.	$T_{m(1)}$	$\Delta H_{(1)}$	$T_{m(2)}$	$\Delta H_{(2)}$	$T_{m(3)}$	$\Delta H_{(3)}$	Lit. Mp ^a	Mp ^b
1a TMC ₁₆ CO ₂ H	196.9	41.5	233.6	66.3	–	–	218 ^c	230 ^c (CTAB)
1b TETC ₁₆ CO ₂ H	77.0	50.4	–	–	–	–	na	177 ^c (CTEAB)
1c TPrC ₁₆ CO ₂ H	77.7	9.6	–	–	–	–	na	120 ^d (CTPrAB)
1d PyC ₁₆ CO ₂ H	180.0	164.5	–	–	–	–	na	70 ^c (CPyAB)
2a TMC ₁₆ OH	113.2	20.8	150.2	46.8	212.3	65.2	217 ^c	230 ^c
2b TETC ₁₆ OH	130.9	22.8	–	–	–	–	159 ^c	177 ^c
2c TPrC ₁₆ OH	85.7	104.8	–	–	–	–	na	120 ^d
2d PyC ₁₆ OH	92.6	38.6	132.0	13.8	150.5	1.22	155 ^c	70 ^c

^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 Ref. [22].^d Taken from Ref. [39].**Fig. 2.** (a) Final melting temperatures of compounds **1a–d** and **2a–d** versus headgroup volume.

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 synthesised were comparable to the literature melting points (Table 2).

Melting points taken from literature show that the trimethyl-, triethyl- and tripropyl-hexadecylammonium bromides display a linear decrease in T_m with head-group size (Fig. 2). This is most probably a reflection of the increasing negative effect of the head-group 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 head-group volumes. Despite the similar size in ammonium headgroup volume between the pyridyl-derivatives (68 Å³) and the trimethyl-(71 Å³) derivatives, the pyridyl compounds do not present any clear trend in melting behaviour when compared to the trialkyl-analogues or themselves as a series.

T_K values were determined for all the bolaform amphiphiles in dilute aqueous solutions (1% w/v) with the T_K being recorded when complete dissolution of the sample in a stirred solution was observed. The averages of the T_K s obtained from 3 measurements of sample solutions at pH 2.2, 7.0 and 11.5 are given in Fig. 3. The T_K s for bolaform amphiphiles at pH 7.0 in all cases were 20–50 °C higher than those for the analogous simple hexadecyl trialkylammonium bromides. This largely correlates with data from Hayman

et al. with the T_K s in general agreement with the previously recorded values (**2a**, **2b**, **2d** and **1a**, Table SI 2 in supporting information) [22,30].

Of particular note are the low T_K s (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 T_K s than CTAB (T_K = 25 °C). However the majority of the bolaform amphiphiles tested (**2b–d**, **1a,b,d**) possessed T_K s 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 T_K s 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 64.3 °C). Differences in T_K s 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 Fig. 4 (the other plots are given in Supporting information) and the results are given in Table 3.

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, CTEAB, 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 (Table 3). 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 mmol dm⁻³ 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 it should be noted that direct comparison between the cmc values is difficult since they were recorded at widely different temperatures as a consequence of their disparate T_K values. Cmc values for ionic surfactants typically initially decrease with increasing T then increase upon further heating, with a minimum cmc value ca. 20–30 °C [73–78]. However the difference in values across the T ranges studied is relatively low and could not account for the difference in values between the bolaform amphiphiles studied here and the analogous ammonium analogues.

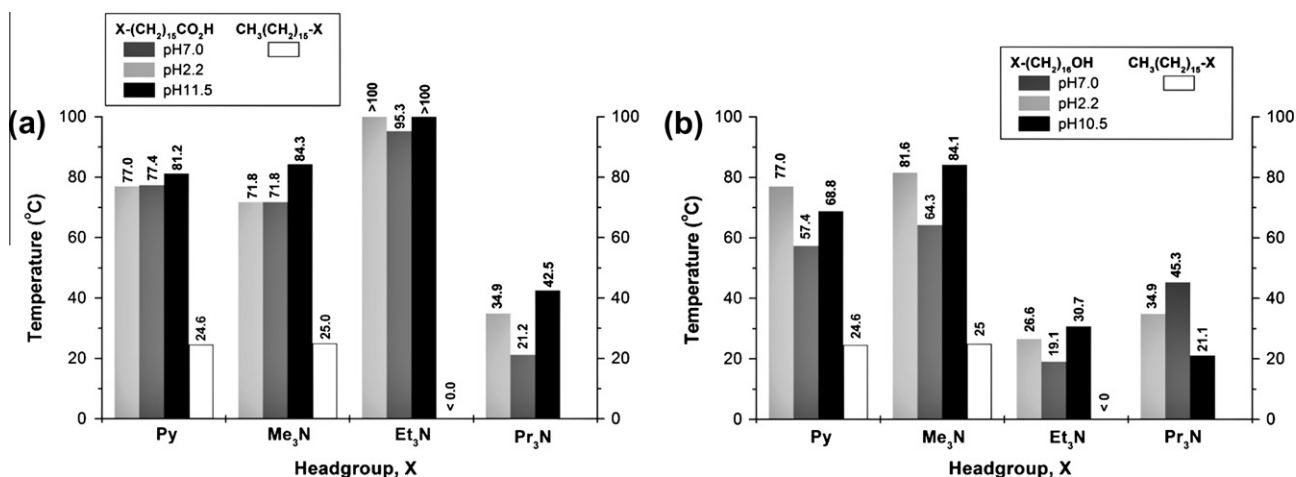


Fig. 3. Krafft temperatures for the ω-carboxy bolaform amphiphiles **1a–1d** and ω-hydroxy bolaform amphiphiles **2a–2d**. **1b** was found to have a Krafft temperature above 100 °C and consequently could not be accurately measured. Error bars not included (<0.1% standard deviation from 3 measurements).

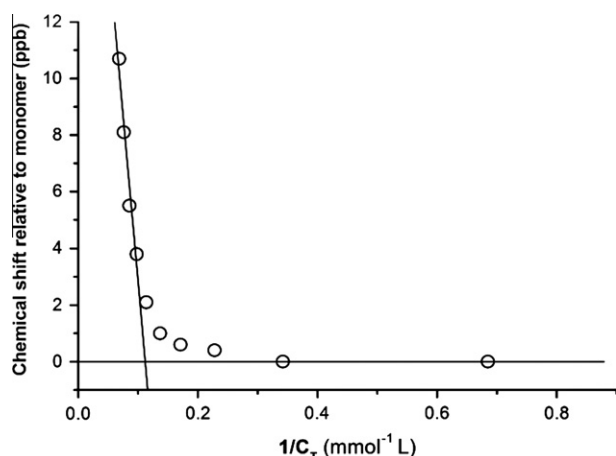


Fig. 4. Chemical shift (relative to monomer) versus $1/C_T$ for NCH₃ headgroup protons of **2a** in D₂O. Cmc taken from the point at which the two lines intersect.

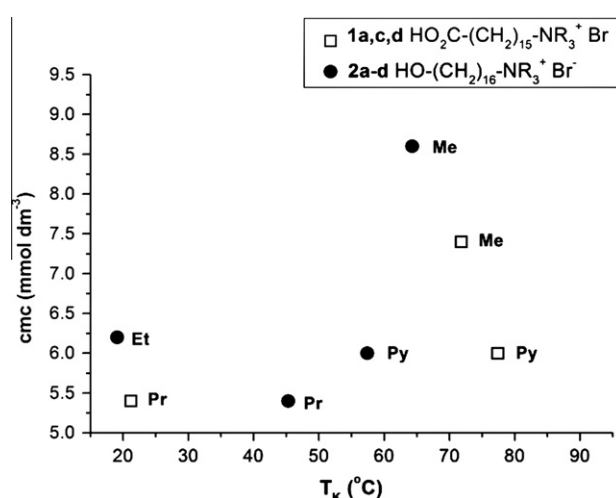


Fig. 5. A plot of T_K versus cmc for the bolaform amphiphiles **1a, c, d** and **2a–d**.

Table 3

Critical micelle concentrations **1a,c,d** and **2a–2d**.

Compound	Cmc (mmol dm ^{−3})		
	This study	T (°C) ^a	Lit.
CTAB	–	–	0.86–1.55 ^b
CTEAB	–	–	0.73 ^c
CTPAB	–	–	0.14–0.58 ^d
PyC ₁₆ Cl	–	–	0.67–1.38 ^e
1a TMC ₁₆ CO ₂ H	7.4	82	9.7 ^f
1b TETC ₁₆ CO ₂ H	–	–	–
1c TPrC ₁₆ CO ₂ H	5.4	31	–
1d PyC ₁₆ CO ₂ H	6.0	87	–
2a TMC ₁₆ OH	8.6	84	9.4 ^g
2b TETC ₁₆ OH	6.2	29	6.2 ^h
2c TPrC ₁₆ OH	5.4	55	–
2d PyC ₁₆ OH	6.0	67	5.9 ⁱ

^a Temperature cmc measured at; in all cases $T_K + 10$ °C.

^b Taken from Refs. [21,30,68].

^c Taken from Refs. [51,63].

^d Taken from Refs. [51,69,70].

^e Taken from Refs. [21,68].

^f Taken from Refs. [21].

No clear relationship was observed between T_K and cmc for the compounds (Fig. 5) and it is possible to conclude that the relative solubility (hydrophobic–lipophilic balance) does not appear to be

relevant in predicting T_K (in line with the hypothesis of Hayman et al.). 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 T_K s. 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 stabilising interactions for the crystal structure of **2a** were postulated to be responsible for its increased T_K (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 T_K 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

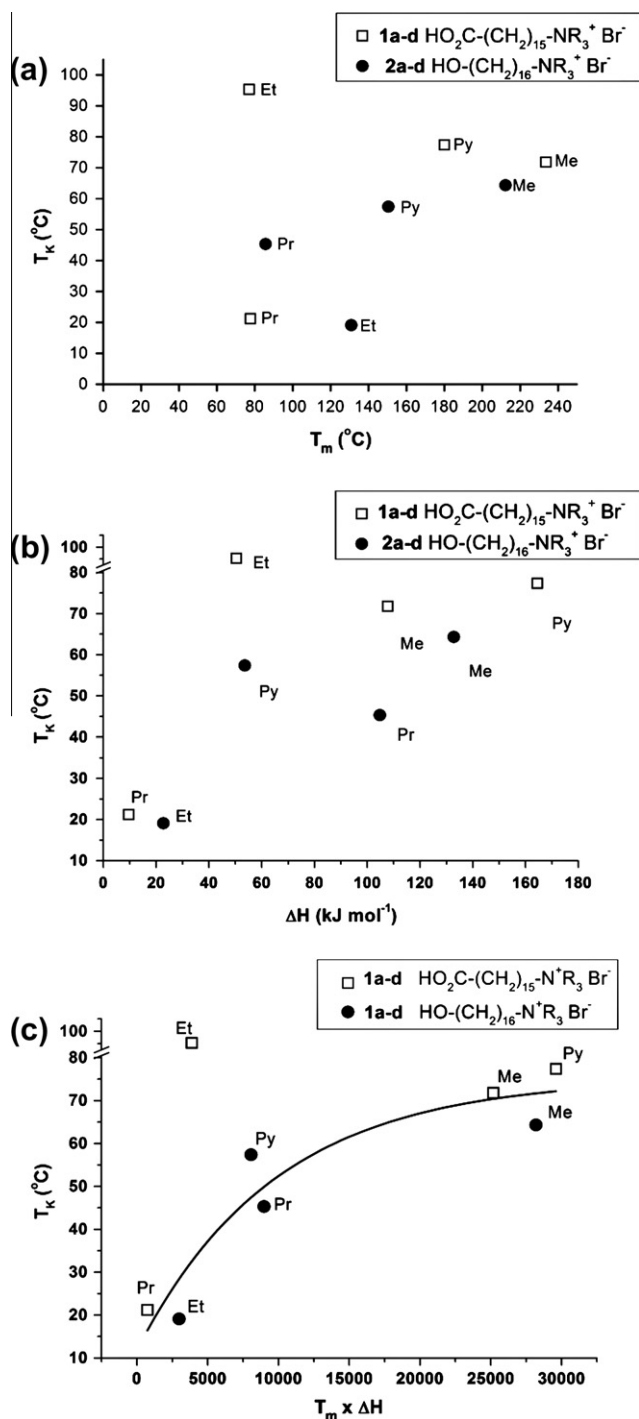


Fig. 6. Variation in Krafft temperatures with (a) melting points, (b) enthalpies and (c) the product of T_m and ΔH for compounds **1a-d** and **2a-d**.

temperatures [22]. A plot of T_m taken from the thermal analyses of the bolaform amphiphiles (Table 2) versus T_K for these amphiphiles is given in Fig. 6a and the plot of T_K versus of the total enthalpy for all transitions between 50 °C and T_m is given in Fig. 6b.

As can be seen there is some correlation between T_m and T_K for all compounds with the exception of **1b** (TetC₁₆CO₂H) and a rougher correlation between T_K and ΔH for all compounds again with the exception of **1b**. Generally the lower the T_m and/or ΔH the lower the T_K . To attempt to take both ΔH and T_m into account in predicting T_K a plot of the product of these two properties is given in Fig. 6c. A considerable reduction in scatter and a clear trend is

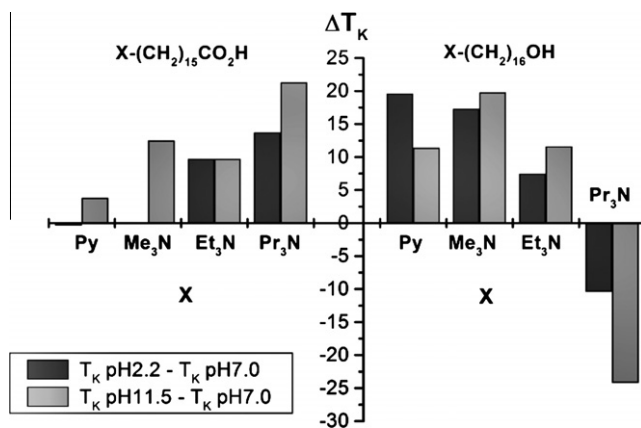


Fig. 7. Effect of pH on the Krafft temperatures of compounds **1a-d** and **2a-d** with respect to pH 7.0.

observed with the exception of **1**; a 1st order exponential decay curve fit gives $T_K \propto \exp(\Delta H * T_m)$. 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 its T_K and the relationship between T_K and $\Delta H * T_m$ is worthy of consideration in the future prediction of Krafft temperatures. However the clearly anomalous behaviour of compound **1b** remains unexplained.

One application of α,ω -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 T_K of our bolaform amphiphiles occurred under these conditions. Surprisingly only a single study has previously reported on the effect of pH on the T_K s of long chain alkyl ammonium salts [32]. In that case it was reported that an increase in pH led to a decrease in the T_K of dodecyl ammonium chloride. The T_K s were measured for all of our compounds at pH 2.2 and 10.5 where the results were given in Fig. 3. The differences in T_K in these pHs and those recorded at pH 7.0 are given in Fig. 7. It can be observed that for almost all of the compounds the differences in pH resulted in an increase in T_K . Given the ionisable nature of carboxylic acid function it was surprising that pH had greater overall effect on the T_K s 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 T_K s for ammonium amphiphiles and this is observed for all but one of the bolaform amphiphiles (**2d**).

3.3. The nature of the bolaform amphiphile aggregates

The aggregation numbers (N_{agg}) of compounds **1a**, **c**, **d** and **2b-d** in D₂O were determined 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. N_{agg} values were determined using the single-step equilibrium model where a plot of $\ln(C_T \delta_{obs})$ against $\ln[C_T(\delta_{mic} - \delta_{obs})]$ gives a

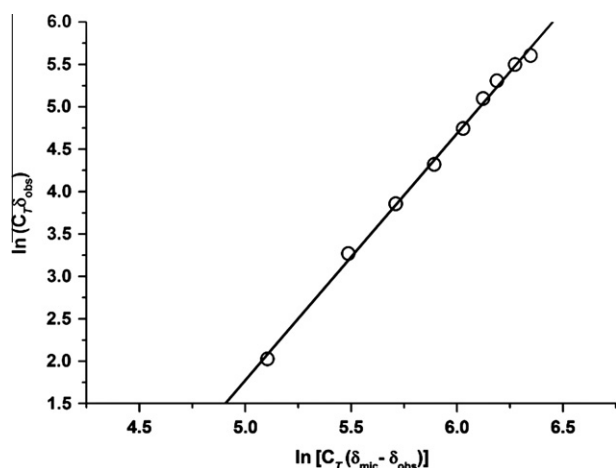


Fig. 8. Representative plot of $\ln(C_T \delta_{\text{obs}})$ against $\ln[C_T (\delta_{\text{mic}} - \delta_{\text{obs}})]$ for **1c** (TPC₁₆OH); the aggregation number was determined from the slope of the linear regression.

straight line with a slope equal to the aggregation number N_{agg} [21,36–38]. An example of a plot resulting from the measurements is shown in Fig. 8 for the amphiphile **2c** (further plots are given in Supporting information). N_{agg} for **1b** could not be determined because of its high T_K but the aggregation numbers of **1a**, **c**, **d** and **2a–d** are given in Table 4. Our values for **2a**, **2b**, **2d** and **1a** are in good agreement with those previously obtained by Hayman et al. (Table 4) and all of the amphiphiles clearly showed substantially smaller aggregation numbers ($N_{\text{agg}} = 2.9$ – 6.7) than their analogous hexadecyl ammonium bromides ($N_{\text{agg}} = 43$ – 104) (Table 4).

Dynamic light scattering was used to measure the apparent hydrodynamic diameters (D_H) of compounds **1a**, **1c**, **1d** and **2a–d** as 1wt% (>cmc) aqueous solutions and representative overlays of frequency counts are given in Fig. 9 and the average results are given in Table 4. 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 N_{agg} from the D_H values required an estimation of the molecular volumes of the bolaform amphiphiles and

whilst a number of values exist in the literature 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 V_{calc}^1 and N_{agg}^1 [49]. For comparison the Connolly excluded volumes (calculated using Chem3D from Cambridgesoft) were used in the calculation of V_{calc}^2 and N_{agg}^2 (Table 4). The volumes of the aggregates were calculated from the D_H values ($4/3\pi(D_H/2)^3$) and they are therefore the theoretical maximum values from the DLS measurements. The N_{agg}^1 and N_{agg}^2 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.

The chain length (l) for the hydrocarbon chains of **1a–d** and **2a–d** can be calculated from $l = 0.2765 + 0.1265 \cdot n\text{CH}_2$ [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 Fig. 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 (Fig. 1). This maximum micellar diameter corresponds to approximate aggregation numbers of between 20 and 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 N_{agg} 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 summarised schematically in Fig. 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 aggre-

Table 4

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

Compound	N_{agg} (NMR)		D_H (Å) ^c	V_{calc}^1 (nm ³) ^d	Theor. N_{agg}^1 ^e	V_{calc}^2 (nm ³) ^f	Theor. N_{agg}^2 ^g	A_{agg} (nm ²) ^h	Theor. N_{agg}^3 ⁱ
	This study ^a	Lit. ^b							
CTAB	–	88–104, 61, 69	–	–	–	–	–	–	–
CTEtAB	–	43, 60	–	–	–	–	–	–	–
CTPrAB	–	40–70, 53	–	–	–	–	–	–	–
CPyAB	–	95	–	–	–	–	–	–	–
1a TMC ₁₆ CO ₂ H	3.9 (0.1)	6 ± 4	2.33 (0.58)	0.356	18.7	0.228	28.3	17.1	28.0
1b TETC ₁₆ CO ₂ H	–	–	–	–	–	–	–	–	–
1c TPrC ₁₆ CO ₂ H	3.5 (0.8)	–	2.10 (0.16)	0.456	10.6	0.257	18.1	13.8	13.8
1d PyC ₁₆ CO ₂ H	2.9 (0.1)	–	2.36 (0.03)	0.358	19.3	0.288	23.0	17.6	27.4
2a TMC ₁₆ OH	5.9 (1.4)	5 ± 2	1.21 (0.36)	0.354	2.6	0.234	4.0	4.60	7.7
2b TETC ₁₆ OH	6.7 (1.7)	11 ± 2	1.44 (0.36)	0.404	3.9	0.229	6.8	6.51	7.8
2c TPrC ₁₆ OH	2.9 (0.1)	–	1.07 (0.12)	0.454	1.4	0.267	2.4	3.59	3.6
2d PyC ₁₆ OH	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 Refs. [30,31,71,72].

^c Hydrodynamic diameter (volume) measured by DLS (average 3+ measurements) at >5 °C above T_K ; standard deviation given in brackets.

^d Molecular volumes of bolaform amphiphiles calculated from partial molar volumes in Ref. [49].

^e $N_{\text{agg}}^1 = (4/3\pi(D_H/2)^3)/V_{\text{calc}}^1$.

^f Connolly excluded volumes of bolaform amphiphiles calculated using Chem3D (Cambridgesoft).

^g $N_{\text{agg}}^2 = (4/3\pi(D_H/2)^3)/V_{\text{calc}}^2$.

^h $A_{\text{agg}} = 4\pi(D_H/2)^2$.

ⁱ $N_{\text{agg}}^3 = (A_{\text{agg}}/A_{\text{headgroups}})$ where $A_{\text{headgroup}}$ = head group limiting areas taken from [60,52–54].

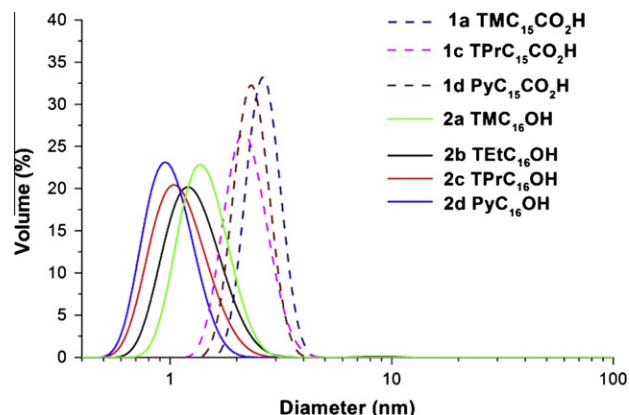


Fig. 9. Typical aggregate size (volume) distributions measured using DLS.

gate-water interface for the ammonium and acid groups forcing an expanded interface relative to volume. However the calculated aggregation numbers (N_{agg}^3 in Table 4) based on the calculated surface area (A) calculated from the D_H 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 (N_{agg}^3 values are close to those predicted by volume calculations (i.e. $N_{agg}^3 \approx N_{agg}^2$).

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 ω -hydroxy bolaform amphiphiles **2a–d** could also not be determined as primary aliphatic hydroxyl groups have pKas of around 15–17 [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 pKa 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-headgroup derivatised analogues. It has also been reported that the incorporation of very hydrophobic alkanolic 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 stabilising the whole micelle by acid ionisation and furthermore increasing the acidity of the solutions (compared to pure solutions of the acids) by charge neutralisation 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

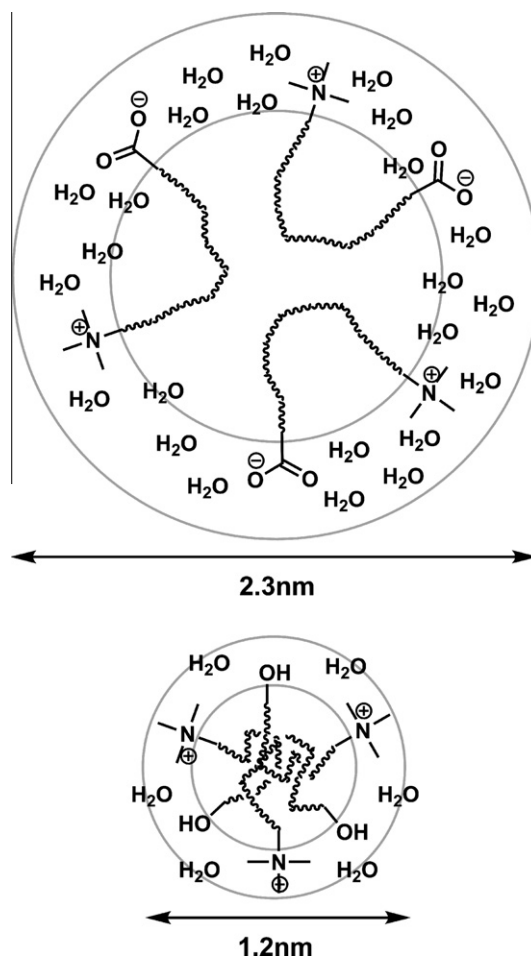


Fig. 10. Tentative models for the micellar aggregates formed by **1a** and **2a**.

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 Fig. 10.

A further important feature in all of DLS measurements was the monomodal nature of the aggregates, whilst larger peaks were observed (~100 nm and ~1000 nm) 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 ca. 1 nm in diameter were possibly present. Thus for all cases a single sized aggregate species is present (>99% in number) with diameters of less than 3 nm (by DLS and TEM) and $N_{agg} < 10$. 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 1 nm to 1 μ 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 ($N_{\text{agg}} < 10$).

4. Conclusions

It has been possible to synthesise eight bolaform compounds and undertake their systematic characterisation. Overall the T_K s of the eight amphiphiles were high with 6 of the eight possessing T_K s greater than 45 °C. Thus most of the amphiphiles could only expect to find application at raised temperatures limiting their potential utility. However in addition to α,ω -hydroxy-hexadecyl triethylammonium bromide (**2b**) with a T_K of 19.1 °C, another amphiphile, α,ω -carboxy-hexadecyl tripropylammonium bromide (**2c**) has been identified with a T_K near ambient temperatures, T_K of 22.1 °C. This provides an acid functional ammonium bolaform amphiphile that micellises at ambient temperatures to complement the hydroxyl. No definitive relationship was observed between the T_K s of the eight bolaform amphiphiles and the structure of their headgroups and no correlation between the amphiphile cmcs and T_K s was observed. A good correlation between T_K and the product of the enthalpies and melting temperatures of the compounds was observed for 7 of the eight compounds, but further and more extensive experiments are needed to determine the general validity of this observation. These observations support previous observations that T_K s are determined by the crystal stability of the bolaform amphiphiles rather than their relative solubilities. Considerable change of the amphiphiles T_K s for different pHs (pH = 2.2 and pH = 11.5) was observed. For 7 of the compounds pH either had no effect or increased T_K by up to 20 °C; the remaining compound showed a decrease in T_K . 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 ($N_{\text{agg}} < 10$). 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 N_{agg} 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 denser micellar type aggregates for the hydroxyl-compounds. We postulate that this 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].

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Appendix A. Supplementary material

Supporting information includes representative DSC chromatograms, thermal data from DSC cooling runs and all plots used to obtain cmc values and N_{agg} values from NMR measurements. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.jcis.2011.10.017.

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