

Research Article

A convenient laboratory synthesis of deuterium-labelled trimethyl tetradecyl ammonium sulphate

Sameer Chavda, Gregory S. Coumbarides, Marco Dingjan, Jason Eames* and Ali Zarbakhsh

School of Biological and Chemical Sciences, Queen Mary, University of London, London E1 4NS, UK

Summary

A convenient and practical laboratory synthesis of deuterium-labelled trimethyl tetradecyl ammonium sulphate is reported. Copyright © 2005 John Wiley & Sons, Ltd.

Key Words: ammonium salts; tetradecyl bromide; deuterium; surfactants; trimethylamine

Introduction

Resolving structures at buried liquid–liquid interfaces contributes to our current understanding of many important processes, such as the transport properties of cell membranes and the stabilisation of emulsions used for drug delivery. The recent development of a novel, versatile and complementary approach for probing the structure of adsorbed polymers and surfactants at oil–water interfaces using neutron reflectometry has made inroads in this area.^{1,2} A preliminary investigation of the interface between an aqueous solution of tetradecyl trimethylammonium bromide (C₁₄TAB) at critical micelle concentration and hexadecane³ posed several intriguing questions regarding the nature of the structure at the oil–water interface. In order to determine adsorbed amounts, the oil and water distributions through the interface need to be known. However, regardless of the underlying oil and water distributions, the nature of the amphiphile distribution raises the most interest. If a single-layer model is used to model the data, the adsorbed amount is significantly less than that found at the air–solution interface,⁴ whereas, one

*Correspondence to: J. Eames, Department of Chemistry, University of Hull, Cottingham Road, Kingston upon Hull, HU6 7RX, UK. E-mail: j.eames@hull.ac.uk

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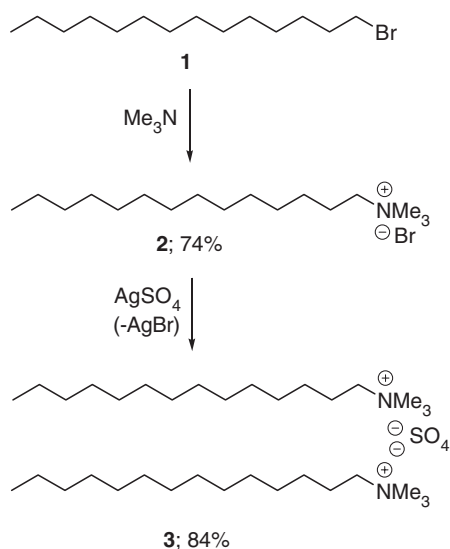
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might have expected the adsorbed amount to be comparable or possibly greater when both segments of the amphiphile are solvated. Furthermore, to obtain both a good fit to the data and an adsorbed amount in the primary adsorbed film that is comparable to that found at the air–solution interface, it is necessary to include a water-rich secondary adsorbed layer. Inclusion of this unexpected layer leads to an excellent fit to the data.

In order to resolve the structure of a water-rich secondary adsorbed layer using neutron reflectometry, isotopic substitution with appropriate deuterium labelling is essential. This would help to determine the adsorbed amount and to examine the oil, water and amphiphile distributions through the interface. In this paper, we report a user friendly and practical route for the synthesis of D-labelled ammonium salts that can be carried out safely by a non-synthetic chemist.

Results and discussion

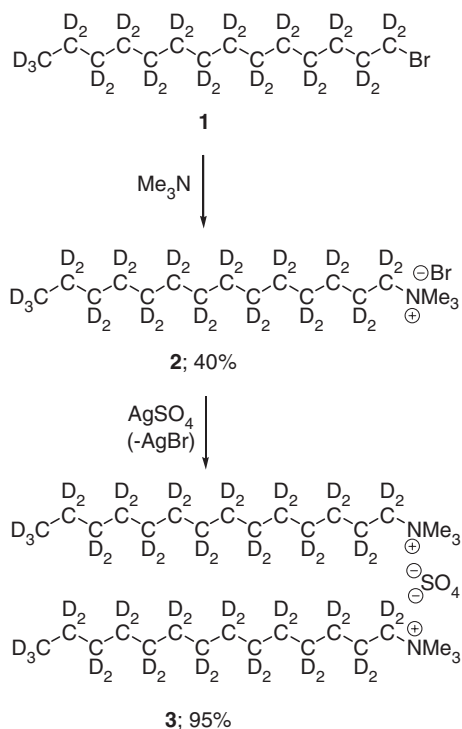
With this aim in mind, we chose to synthesize the required unlabelled ammonium salt, trimethyl tetradecyl ammonium bromide **2**,⁵ by sequential addition of four equivalents of trimethylamine (b.p. 3–4°C) to neat 1-bromotetradecane **1** at 0°C under a nitrogen atmosphere. The resulting solution was stirred for 12 h to give a crude residue of trimethyl tetradecyl ammonium bromide **2**. This was subsequently purified through precipitation, by addition of acetone, to give the required trimethyl tetradecyl ammonium bromide **2** as a white powder in 74% yield (Scheme 1). It is interesting to note, by placing the reaction vessel under a positive pressure of nitrogen (by using a balloon of nitrogen) considerably reduced the volatility of the trimethylamine (b.p. 3–4°C).



Scheme 1.

Our attention next turned towards the synthesis of the trimethyl tetradecyl ammonium sulphate **3** by substituting the bromide counter in the ammonium bromide **2** with a sulphate counter. This was achieved using a modified route,⁵ by addition of silver sulphate (0.5 equiv.) to a stirred solution of ammonium bromide **2** (1 equiv.) in water (Scheme 1). This solution was stirred for 20 min and the resulting grey precipitate (silver bromide) was removed through filtration. Acetone was added to the filtrate to assist precipitation of the remaining silver bromide, which was removed through decanting. The final traces of silver bromide were removed through double filtration using a cotton-wool pipette. Evaporation of the colourless acetone–water layer gave, after sequential addition of dry acetone to remove the final traces of water, the required trimethyl tetradecyl ammonium sulphate **3** as a white powder in 84% yield (Scheme 1).

With this information in hand, we next turned our attention towards the synthesis of the corresponding deuterium-labelled trimethyl tetradecyl ammonium sulphate **3-*d*₂₉**. We chose to use the commercially available deuterium-labelled bromotetradecane **1-*d*₂₉** as our starting precursor (Scheme 2). Using our previously outlined protocol, the required trimethyl tetradecyl ammonium bromide **2-*d*₂₉** and sulphate **3-*d*₂₉** were economically synthesized on a small laboratory scale (0.5–2.0 mmol scale) from the corresponding



Scheme 2.

bromide **1-d₂₉**, in 40 and 57% yields, respectively (Scheme 2). It is interesting to note, the melting points for these unlabelled and deuterium-labelled sulphates, **3** and **3-d₂₉** were different, which was presumably due to the changes within their lattice energies. Our neutron diffraction studies of these samples will be published in due course.

Experimental

All reactions were carried out under nitrogen using oven-dried glassware. Proton and carbon NMR spectra were recorded on a Bruker AM 400 Fourier transform spectrometers using an internal deuterium lock. Chemical shifts are quoted in parts per million downfield from tetramethylsilane. Carbon NMR spectra were recorded with broad proton decoupling. Infrared spectra were recorded on a Shimadzu 8300 FTIR machine. The levels of D-incorporation were determined by a combination of mass and proton NMR spectra.

Trimethyl tetradecyl ammonium bromide 1⁵

Trimethylamine (0.47 g, 0.65 ml, 7.9 mmol) was added to neat 1-bromotetradecane **1** (2 g, 2.15 ml, 7.2 mmol) at 0°C and the resulting solution was stirred for 4 h. Three further portions of trimethylamine (0.47 g, 0.65 ml, 7.9 mmol) were added to this solution after 4-h intervals. The resulting solution was left to stir for a further 12 h. The resulting residue was purified by the addition of acetone to give the ammonium salt **2** (1.8 g, 74%) as white crystalline solid; mpt > 230°C; δ_{H} (400 MHz, CDCl₃) 3.45 (2 H, m, CH₂N), 3.20 (9 H, s, 3 × CH₃), 1.80 (2 H, m, CH₂), 1.40 (6 H, br m, 3 × CH₂), 1.32 (18 H, m, 9 × CH₂) and 0.90 (3 H, t, $J = 6.9$ Hz, CH₃CH₂); δ_{C} (100 MHz, CDCl₃) 66.5 (CH₂N), 53.2 (CH₃N), 32.1 (CH₂), 30.1 (2 × CH₂), 30.0 (CH₂), 29.9 (CH₂), 29.8 (CH₂), 29.6 (CH₂), 29.3 (CH₂), 26.3 (CH₂), 22.9 (CH₂), 22.7 (2 × CH₂) and 13.9 (CH₃) (found C₁₇H₃₈N⁺, 256.2999. C₁₇H₃₈N requires M, 256.2999).

Trimethyl tetradecyl ammonium bromide 2-d₂₉

Using the same method as the ammonium salt **2**, trimethylamine (0.47 g, 0.65 ml, 7.9 mmol; four portions of 0.47 g, 0.65 ml, 7.9 mmol) and 1-bromotetradecane **1-d₂₉** (0.5 g, 1.63 mmol), gave the deuterium-labelled ammonium salt **2-d₂₉** (0.23 g, 40%) as a white; mpt > 230°C; ν_{max} (film)/cm⁻¹ 2150–2100 (CD); δ_{H} (400 MHz, CDCl₃) 3.11 (9 H, s, 3 × CH₃); δ_{C} (100 MHz, CDCl₃)[†] 53.0 (CH₃N) (found C₁₇H₉D₂₉N⁺, 285.4817. C₁₇H₉D₂₉N requires M, 258.4819).

[†]The absence of defined multiplets for CD₂ and CD₃ groupings (within the ¹³C NMR spectrum) is presumably due to a combination of long relaxation times for the associated carbon nuclei, and low solubility of the parent ammonium salt in deuteriochloroform. For additional information see Eames *et al.*⁶

*Trimethyl tetradecyl ammonium sulphate 3*⁵

Silver sulphate (93 mg, 0.29 mmol) was added to a stirred solution of ammonium salt **2** (0.2 g, 0.59 mmol) in water (3 ml) at room temperature. The resulting solution was stirred for 30 min to give a cream coloured solution. The residual silver bromide was filtered off to give a light grey solution. Acetone (20 ml) was added to assist the precipitation of the remaining silver bromide, which was removed by decanting into another flask. The remaining solution was filtered twice through a pipette column packed with cotton wool, evaporated under reduced pressure by sequential addition of acetone (to aid removal of the resulting water) to give the ammonium sulphate **3** (0.15 g, 84%) as a white crystalline solid; mpt 207–210°C; δ_{H} (400 MHz, CDCl₃) 3.16 (2 H, m, CH₂N), 2.99 (9 H, s, 3 × CH₃), 1.61 (2 H, m, CH₂), 1.22 (6 H, br m, 3 × CH₂), 1.16 (18 H, m, 9 × CH₂) and 0.73 (3 H, t, $J = 6.8$ Hz, CH₃CH₂); δ_{C} (100 MHz, CDCl₃) 66.5 (CH₂N), 52.9 (CH₃N), 31.9 (CH₂), 30.2 (2 × CH₂), 30.0 (CH₂), 29.9 (CH₂), 29.8 (CH₂), 29.7 (CH₂), 29.5 (CH₂), 26.1 (CH₂), 22.9 (CH₂), 22.7 (2 × CH₂) and 13.9 (CH₃) (found C₁₇H₃₈N⁺, 256.3002. C₁₇H₃₈N requires M, 256.2999).

Trimethyl tetradecyl ammonium sulphate 3-d₂₉

Using the same method as the ammonium sulphate **3**, silver sulphate (89 mg, 0.28 mmol) and the ammonium salt **2-d₂₉** (0.211 g, 0.57 mmol), gave the deuteriated ammonium sulphate **3-d₂₉** (0.18 g, 95%) as a white solid; mp = 210–212°C; ν_{max} (film)/cm⁻¹ 2160–2090 (CD); δ_{H} (400 MHz, CDCl₃) 3.99 (9 H, s, 3 × CH₃); δ_{C} (100 MHz, CDCl₃)⁶ 52.8 (CH₃N) (found C₁₇H₉D₂₉N⁺, 285.4817. C₁₇H₉D₂₉N requires M, 258.4819).

Acknowledgements

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