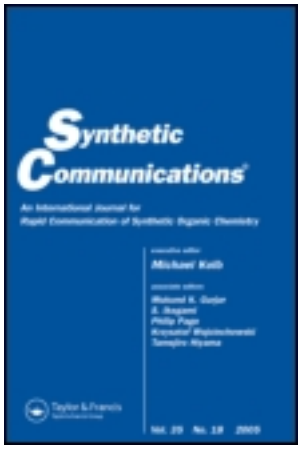

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SYNTHESIS OF ADAMANTANE-BASED TRIMERIC CATIONIC SURFACTANTS

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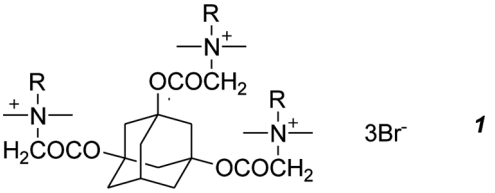
GRAPHICAL ABSTRACT



1a,R=C_8; 1b,R=C_{10}; 1c,R=C_{12}

Abstract *Three trimeric quaternary ammonium surfactants, having adamantane cores and different carbon chains, were synthesized using adamantane as the starting raw material. The target compounds were confirmed by elemental analysis, ^1H NMR, ^{13}C NMR, and mass spectroscopy. The influences of reaction conditions on the yields of the key intermediate product 1,3,5-trihydroxyadamantane (***3***) were investigated. Surface properties of the target compounds were measured. The critical micelle concentration values of* **1a**, **1b**, *and* **1c** *were 2 mM, 1 mM, and 0.5 mM, respectively.*

Keywords Adamantane; critical micelle concentration; trimeric cationic surfactant

INTRODUCTION

In recent years, the unusual qualities such as high surface activity, low critical micelle concentration (CMC), and diverse aggregate structures of Gemini surfactants, which contain double hydrophobic chains and hydrophilic headgroups linked by spacer groups, have been realized.[1–5] This has raised questions about the behavior of higher oligomeric analogs.[6,7] However, only a limited number of trimeric surfactants have been synthesized and studied so far, even though the properties of

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oligomeric surfactants have been found to be better than corresponding dimeric homologs.[8–10] Recently a few kinds of trimeric quaternary ammonium halide surfactants with different spacer groups were synthesized and investigated.[11–15] It was found that the spacer groups exerted important influence on the behavior of oligomeric surfactants.

Adamantane is a highly symmetric cage-like hydrocarbon with the molecular formula $C_{10}H_{16}$, where the six methylene groups form an octahedron and the four methane groups projecting out form a tetrahedron.[16,17] The special structure of adamantane gives it many useful chemical and physical properties, such as high boiling point, good thermal stability, and nontoxicity. The bridge carbon atoms of adamantane are active, which allows substitution, oxidation, and alkylation reactions to take place, producing a wide variety of adamantane derivatives.[18] This make adamantane devisable and able to be used as the spacer of oligomeric surfactants, which may have low CMC value, high antibacterial properties, and foam performance.

In this article, adamantane was used as the spacer group to synthesize a trimeric quaternary ammonium halide surfactant. To make the target trimeric cationic surfactant degradable, bromoacetyl bromide was introduced into the adamantane structure to produce ester groups after the hydroxylation reaction of adamantane. Subsequently the alkyl (alkyl = C_8, C_{10}, C_{12}) tertiary amines in which the alkyl groups acted as hydrophobic building blocks were connected to the spacers by a quaterization reaction to give the corresponding quaternary amine trimeric surfactants. Additionally, the CMC of the synthesized trimeric cationic surfactants was measured. The antibacterial property and foam performance will be reported elsewhere.

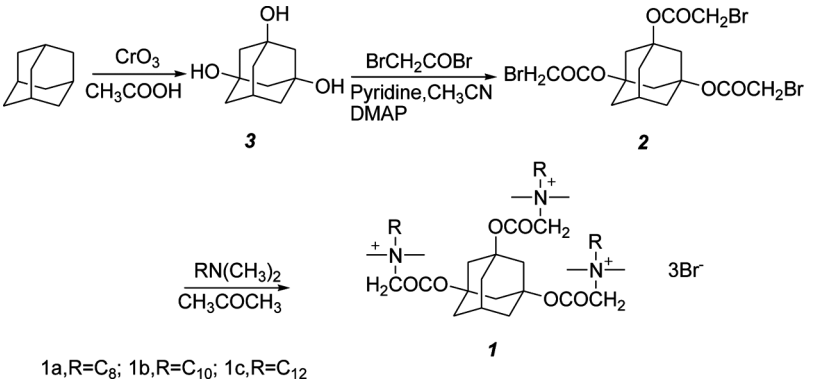
RESULTS AND DISCUSSION

Synthesis

To make the target compounds easy to degrade, the trimeric cationic surfactants were designed to contain ester groups, and thus the target compounds were synthesized in the following steps: First, the adamantane spacer was oxidized by chromium trioxide to produce 1,3,5-trihydroxyadamantane **3**. Then the 1,3,5-trihydroxyadamantane **3** was esterized by bromoacetyl bromide to give 1,3,5-trikis (bromoacetoxy)adamantane **2**. Subsequently three alkyl (alkyl = C_8, C_{10}, C_{12}) tertiary amines were connected to the spacers by quaterization to give the corresponding quaternary amine cationic surfactants **1** (shown in Scheme 1).

Influences of Reaction Conditions

The last two steps were classical reactions and had excellent yield without optimization in this study, whereas on the first step reaction, the oxidation conditions of adamantane including molar ratio of CrO_3/adamantane (ADH), temperature, and reaction time were investigated. For the oxidation reaction of adamantane, several oxidizing agents have been reported, including hypochlorous acid and methyl (trifluoromethyl)dioxirane.[19,20] However, both of them had some shortcomings. The selectivity and yield of the reaction using hypochlorous acid as oxidizing agent were quite poor, and difficult to separate, and the other oxidizing agent is expensive



Scheme 1. Synthesis of **1**.

and unstable. Therefore, in this article, another oxidizing agent, CrO_3, was employed to obtain the intermediate 1,3,5-trihydroxyadamantane (**3**), which had been used by Landa et al. in 1967[21] to oxidize adamantane to form its corresponding single-hydroxy products. The results are shown in Table 1.

The molar ratio of CrO_3 and ADH had a deep effect on the yield of 1,3,5-trihydroxyadamantane. The maximum yield reached 50.1% when the molar ratio was 10, but the yield of **3** decreased as the molar ratio increased. This was because in this oxidation reaction, four products (1-hydroxyadamantane, 1,3-dihydroxyadamantane, 1,3,5-trihydroxyadamantane, and 1,3,5,7-tetrahydroxy-adamantane) can be obtained under different conditions. When the molar ratio of CrO_3 and ADH was 10, the main product was 1,3,5-trihydroxyadamantane **3**, whereas with less oxidation reagent, most of adamantane was oxidated to 1-hydroxy-adamantane and 1,3-dihydroxyadamantane, and with more oxidation reagent, the main product was 1,3,5,7-tetrahydrogxyadamantane.

As most of organic reactions have to be heated, commonly the reaction ratio at low temperature was slow and had poor yield. In this study, it was found that when the oxidation reagent was added to the reaction, temperature would increase and the reaction could happen at 80 °C. However, this temperature was not the optimal

Table 1. Effects of reaction conditions on yield of **3**

No.	CrO_3/ADH (mol ratio)	Temperature (°C)	Time (h)	Yield (%)
1	5	100	3	4.2
2	5	110	2	3.1
3	10	90	1	33
4	10	100	1	50
5	10	110	1	45
6	10	100	2	50
7	10	100	3	49
8	15	100	1	30
9	20	100	1	11

Note. Acetic acid as solvent.

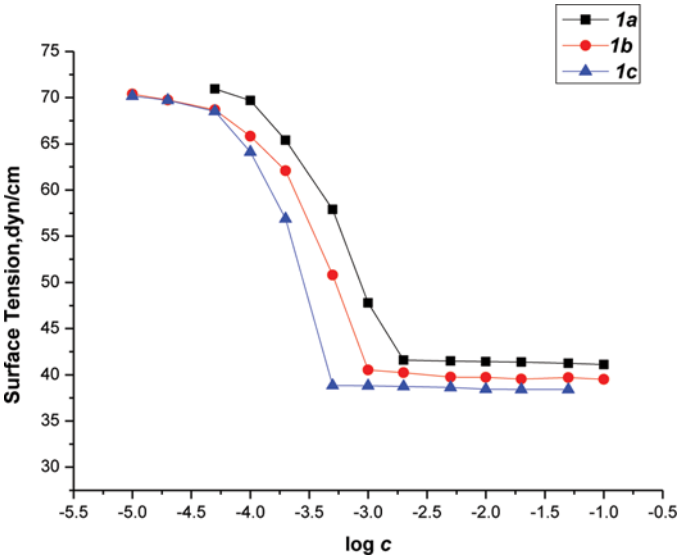


Figure 1. Surface tension of **1** water solutions. (Figure is provided in color online.)

temperature. The subsequent investigation showed that reaction yield was much greater when the reaction temperature was 100 °C, and the yield at 110 °C was less. It may have been caused by the sublimation of adamantane, because more adamantane escaped from the reaction system when temperature above 100 °C, or it might be induced by the ring-opening reaction, which happens more easily at 110 °C.

Furthermore, when the reaction time was more than 1 h, the yield of **3** slowly decreased with prolonged reaction time. The reason for this consequence may be that more adamantane was oxidized to the by-product, 1,3,5,7-tetrahydroxyadamantane.

Surface-Active Properties

CMC is the most common descriptor of surfactant systems. The CMC value is usually detected by plotting surface tension vs log concentration. The surface tension will decrease as the concentration of the solution increases, until it reaches CMC, when a sharp bend appears in the plot. Figure 1 shows the results of the synthesized trimeric surfactant concentrations and their corresponding surface tensions. In Fig. 1 the break points correspond to the CMC of 2 mM, 1 mM, and 0.5 mM, which represents the CMC of the synthesized trimeric surfactants **1a**, **1b**, and **1c** respectively. These values lay far below the CMC of monomeric surfactants (C_8TAB, 290 Mm; C_{10}TAB, 65 mM; and C_{12}TAB, 14.6 mM).[22]

CONCLUSIONS

The trimeric cationic surfactants, 1,3,5-trikis(dimethyl-alkyl-ammonio-acetoxy) adamantane tribromide (alkyl = C_8, C_{10}, C_{12}), were successfully synthesized using adamantane as raw material by oxidation, esterification, and quaterization reactions

successively. Synthesis of 1,3,5-trihydroxyadamantane (**3**) was a crucial reaction. The influences of reaction conditions on the yields of **3** were investigated. It was found that the greatest yield (50.1%) of 1,3,5-trihydroxyadamantane (**3**) could be obtained under the conditions of 100 °C, 1 h, and $CrO_3/ADH = 10$. The CMC of the trimeric cationic surfactants **1a**, **1b**, and **1c** were 2 mM, 1 mM, and 0.5 mM respectively, which were far less than the values of their corresponding monomeric surfactants.

EXPERIMENTAL

Melting points are uncorrected. All reactions were carried out under a nitrogen atmosphere. Solvents were reagent grade and in most cases dried prior to use. All reagents were purchased from Aladdin. Amines were redistilled prior to use. Column chromatography was performed on silica gel 60 (Merk 230 400 mesh). ^{1}H NMR and ^{13}C NMR spectra were recorded on a Varian Mercury-plus 300 spectrometer at 300 MHz and 75 MHz respectively. Mass spectra were recorded on a LCMS-2020 instrument. Tensiometry was performed using freshly prepared solutions with a KSV Sigma 700 tensiometer by the ring method: Each point was tested five times, and the average was used.

Synthesis of 1,3,5-Trihydroxyadamantane 3

A mixture of adamantane (13.6 g, 0.1 mol) and acetic acid (100 g, 1.67 mol) were added to a 200-mL, three-neck flask and stirred at 80 °C. Chromic acid solution, which was prepared by dissolving quantitative chromium trioxide (100 g, 1.0 mol) into 54 mL of water, was added dropwise into the former mixture, and the reaction temperature was kept below 100 °C. Then, the mixture was heated to 100 °C and kept there for 1h. The solvent was removed by vacuum distillation, and sodium hydroxide, solution was added to the residue for neutralization and extracted by boiling ethyl acetate (5×200 mL). The extract was left standing overnight; the white precipitate was obtained by filtration. Yield 8.5 g (50.1%), mp 203–205 °C. ^{1}H NMR (DMSO-d_6, 300 MHz) δ: 4.50 (s, 3H), 2.10 (s, 1H), 1.33–1.42 (m, 12H). Anal. calcd for $C_{10}H_{16}O_3$: C, 65.19; H, 8.75. Found: C, 65.14; H, 8.74.

Synthesis of 1,3,5-Trikis(bromoacetoxy)adamantane 2

A catalytic amount (20 mg) of 4-(dimethylamino)pyridine (DMAP) was added to a stirred suspension of 1,3,5-trihydroxyadamantane (1.47 g, 7.99 mmol) in 2.0 mL of pyridine (24.6 mmol) and 12 mL of CH_3CN. $BrCH_2COBr$ (4.12 mL, 47.2 mmol) was then added dropwise at 0 °C over 1 h. The mixture was stirred and kept at 60 °C for 5 h. After that, the solution became transparent and homogeneous. Six mL of HCl (6 M) was added to the reaction mixture together with 10 mL of CH_2Cl_2. The aqueous layer was extracted with CH_2Cl_2 (3×12 mL), and the combined organic layers were concentrated to give a light-brown liquid residue. The liquid was dissolved in 10 mL of CH_2Cl_2 and washed with brine and 10 mL of aqueous 0.5 M Na_2CO_3. After that the organic layer turned brown-black. This was concentrated and purified by filtering through a silica-gel column. Elution with CH_2Cl_2 gave the desired product as a yellow-white liquid, yielding 3.56 g (82%). ^{1}H NMR ($CDCl_3$) δ: 3.76 (s, 6H), 2.56

(m, 7H), 2.10 (d, 6H); ^{13}C NMR (DMSO-d_6) δ: 168.7, 84.0, 82.4, 62.9, 46.241, 31.3. Anal. calcd. for $C_{16}H_{19}Br_3O_6$: C, 35.13; H, 3.50; Br, 43.82. Found: C, 35.29; H, 3.45; Br, 43.46.

General Procedure for the Preparation of the Trimeric Surfactants

In a round-bottom flask, 1.11 g (2.03 mmol) of 1,3,5-trikis(bromoacetoxy)-adamantane was dissolved in 20 mL of acetone, and was added tertiary amine (9.14 mmol) to the clear solution in one portion. The solution was vigorously stirred for 3 h at 30 °C, during which a white precipitate formed gradually. The precipitate was filtered and then washed several times with acetone to give a white solid.

1,3,5-Trikis(dimethyloctylammonioacetoxy)adamantane tribromide 1*a*. Recrystallized from CH_3CN/acetone: yield 86%; mp 196.1–196.9 °C; ^{1}H NMR (CD_3CN) δ 4.31 (s, 6H), 3.46 (m, 6H), 3.19 (s, 18H), 2.52 (s, 7H), 2.04(s, 6H), 1.65 (m, 6H), 1.33–1.23 (m, 30H), 0.84 (t, 9H, $J = 6.6$ Hz); ^{13}C NMR (DMSO-d_6) δ: 164.3, 82.9, 65.5, 61.7, 51.8, 43.9, 32.1, 29.3, 29.3, 26.5, 22.9, 22.7, 14.6; ESI-MS: 259 (68%) $(M\text{-}3Br)^{3+}$, 429 (100%) $(M\text{-}2Br)^{2+}$. Anal. calcd. for $C_{46}H_{88}Br_3N_3O_6$: C, 54.22; H, 8.71; N, 4.12; Br, 23.53. Found: C, 54.12; H, 8.73; N, 4.29; Br, 23.46.

1,3,5-Trikis(dimethyldecylammonioacetoxy)adamantane tribromide 1*b*. Recrystallized from CH_3CN/acetone: yield 83%; mp 194.8–196.3 °C; ^{1}H NMR (CD_3CN) δ 4.29 (s, 6H), 3.48 (m, 6H), 3.23 (s, 18H), 2.59 (s, 7H), 2.10 (s, 6H), 1.70 (m, 6H), 1.31–1.21 (m, 42H), 0.87 (t, 9H, $J = 6.6$ Hz); ^{13}C NMR (DMSO-d_6) δ: 164.3, 82.9, 65.5, 61.7, 51.8, 43.9, 32.1, 29.7, 29.6, 29.5, 29.3, 26.5, 22.9, 22.7, 14.8; ESI-MS: 288 (100%) $(M\text{-}3Br)^{3+}$, 472 (70%) $(M\text{-}2Br)^{2+}$. Anal. calcd for $C_{52}H_{100}Br_3N_3O_6$: C, 56.62; H, 9.14; N, 3.81; Br, 21.73. Found: C, 56.49; H, 9.23; N, 3.93; Br, 21.65.

1,3,5-Trikis(dimethyldodecylammonioacetoxy)adamantane tribromide 1*c*. Recrystallized from CH_3CN/acetone: yield 80%; mp 193.9–195.7 °C; ^{1}H NMR (CD_3CN) δ 4.25 (s, 6H), 3.45 (m, 6H), 3.19 (s, 18H), 2.56 (s, 7H), 2.08 (s, 6H), 1.68 (m, 6H), 1.33–1.23 (m, 54H), 0.87 (t, 9H, $J = 6.8$ Hz); ^{13}C NMR (DMSO-d_6) δ: 164.3, 82.9, 65.5, 61.7, 51.8, 43.9, 32.1, 29.9, 29.8, 29.6, 29.6, 29.3, 29.3, 26.5, 22.9, 22.7, 14.8; ESI-MS: 316 (100%) $(M\text{-}3Br)^{3+}$, 514 (57%) $(M\text{-}2Br)^{2+}$. Anal. calcd. for $C_{58}H_{112}Br_3N_3O_6$: C, 58.68; H, 9.51; N, 3.54; Br, 20.19. Found: C, 58.59; H, 9.63; N, 3.69; Br, 20.20.

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